THE PRACTITIONER

No. 980 FEBRUARY 1950 Volume 164

THE MONTH

Neurology

NEUROLOGY is probably the section of medicine which has been least affected by the dramatic advances in therapeutics that have taken place during the last two decades. On the other hand it still remains one of the most intellectually stimulating branches of medicine. In our symposium this month we have selected for discussion those neurological disturbances which are either the most common in general practice or are the most difficult for the general practitioner to elucidate when he encounters them. The outstanding omission is a deliberate one—namely, the treatment of Parkinsonism. The reason for this omission is that we felt that sufficient time had not yet elapsed to give even a preliminary authoritative review of the status of such drugs as artane, diparcol and parpanit. We have therefore arranged to publish an article on the "Modern Treatment of Parkinsonism" in "Current Therapeutics" later in the year.

A Great Enterprise

THE national gift for improvization is nowhere better exemplified than in the magnificent way in which the King Edward's Hospital Fund is adapting itself to the entirely new problems with which it has been presented by the initiation of the National Health Service. Now that the hospitals of the country have been taken over by the State, the Fund is devoting its not inconsiderable resources (an investment income of £245,000 per annum) to the development of those essential amenities of a modern hospital for which there is little prospect of a subsidy from the Exchequer. Outstanding among these are the special appropriation of £250,000 for the provision of homes for the aged sick, £100,000 for convalescent homes, and £100,000 for a catering and dietetic training centre which is to be established at St. Pancras Hospital. A further valuable development is the Staff College for Ward Sisters which has been in full use since March 1949. The main aim of this College is to give training for staff nurses about to become ward sisters. This overcomes the former lack in training facilities which allowed staff nurses to be given the charge of wards without adequate knowledge of their new duties. In addition, the Fund has recently established a staff college for hospital administrators in London. These are but a few of the activities of an organization which is clearly determined to demonstrate to the country that there is scope for private enterprise within a national health service. The mellowing influence of work such as this should go far towards humanizing the cold austerity of Whitehall.

The Nuffield Foundation

AN announcement in the medical press last month drew attention to yet another private charity which is adjusting itself admirably to the new regime. The Nuffield Foundation, under the inspiring chairmanship of Sir William Goodenough, has cast its net wide; but with the same abhorrence of redundancy which contributed so much to its founder's fortune, it has consistently used its ample means to finance enterprises which would not otherwise be fully developed. Like the King Edward's Hospital Fund, it has devoted much of its resources to the amelioration of the lot of the aged but, in keeping with Lord Nuffield's own personal wishes, it has also given much thought and attention to medical education. Its medical fellowships, which were advertised in our pages last month, are an excellent example of this, with their wide sphere of usefulness, their minimum of regulations and their generous support of travel abroad. The Foundation's support of social medicine, industrial health, and chronic rheumatism has permitted a development of research into these problems which is already paying handsome dividends, and on which the historian of the future will have much to comment when the story of our generation comes to be written.

Compound E and Vitamin E

FOR those of us reared in the therapeutic nihilism of the first quarter of the century these are exciting days in which we are now living. There is a widespread feeling that, in the words of our American friends, something big is about to break in the field of therapeutics. The observations of the Mayo Clinic workers on the effect of compound E in rheumatoid arthritis, followed by the evidence that the adrenocorticotrophic hormone of the pituitary (ACTH) has a similar effect, has revolutionized our ideas on the whole problem of the etiology of the rheumatic diseases. When these reports are followed by others suggesting that ascorbic acid may play an important part in the control of the same group of diseases, it is clear that we are on the verge of a tremendous step forward in the conquest of one of the remaining outstanding scourges of mankind.

The vitamin E story is not quite such a happy one, but when in one week two leading contemporaries come out with three independent articles suggesting that vitamin E is of value in such a heterogeneous set of conditions as the menopausal syndrome, Dupuytren's contracture, and intermittent claudication, it is evident that the whole problem of the therapeutic status of vitamin E requires careful overhauling. Of its biological significance there can be no doubt, and it is to be regretted that the original claims of the Canadian workers were not couched in more moderate terms. Theorizing in the field of therapeutic applications of physiological principles is always dangerous, but it is not beyond the realm of possibility that vitamin E may yet be found to be of value in the therapeutic control of at least some of the conditions included in the group of disturbances at present included under

the generic umbrella of the rheumatic diseases. It is to be hoped that this problem will in future be tackled in a more scientific manner than it has been in the past.

Medical Television

THE founders of the General Medical Council could never have foreseen the problems of medical advertising which would assail their successors. Television has raised the question in a more acute form than ever before, and although the spirit of the law is much more important than the letter where an honourable profession such as medicine is concerned, it is to be hoped that the G.M.C. will give some guidance in this matter. The educational potentialities of television are such that it must obviously be used for keeping the public informed on medical matters, and it would be a major tragedy if the pick of the profession were not to be available for this purpose. The B.B.C. requirements for the best "televisor" may not always be commensurate with professional standing, but, as at least one performance has already shown, the two are not incompatible.

America and "Socialized Medicine"

THE National Health number of *The Practitioner* has been widely read in the United States, where both doctors and public are very much concerned with the problem of what is usually referred to in that country as "socialized medicine", with its advantages and disadvantages. They are naturally anxious to learn how the scheme is working in Britain, but what they have been told is chiefly what someone or other wishes them to believe. Eloquent emissaries, administrators, doctors or patients, carefully selected and briefed and provided with the dollars to travel and the script to put across, have been telling them of the wonders of a welfare state. On the other hand they have read of the iniquities and mercenary outlook of the British doctor. An example of this kind of propaganda is the story of an American doctor who called on a British colleague, and went with him into his surgery and found a crowd of seventy-five patients waiting. "Hell!" said the Briton. "I shall never finish this lot. Hands up those who have a headache. Now come and get a prescription for headache powders. Hands up those that have a cough. Come and get a cough mixture. Hands up those with bellyache. Here's a purge", and so on until the room was empty and the two went out to dinner. This story would raise a laugh anywhere, but the real laugh is that it is being recited in America as a true story and the name of a senior and respected American doctor is given as having witnessed the incident.

The problems of American Medicine are very different from ours. American doctors will solve their problems in their own way, but they can learn much from what is happening in this country if they are allowed to hear it. There can be little doubt that the more thoughtful of the profession

in the States are paying careful attention to the lessons to be learned from our experience in Great Britain.

"The Times" and "The Practitioner"

THE glory of the English language is its flexibility, but we must confess that we do not yet understand how our plea last month to our fellow editors in Fleet Street for more accurate and adequate medical reporting could possibly be construed as an attack on the English press. *The Times*, with its innate sense of loyalty and rightly aware of its own high standing in such matters, may have felt that it was its duty to rally to the defence of its contemporaries round the corner, but even so the somewhat quixotic twist it gave to our comments seems scarcely justified. What worries us rather more in *The Times*' note is the unfortunate reference to unpunctuality of publication. For the sake of veracity we feel that it is only fair to point out that within living memory *The Practitioner* has only been late in appearing on three occasions. Twice the printing works were bombed during the last war, resulting in complete destruction of the entire issue. The third occasion was during the fuel crisis of 1947, when as a result of a Government edict we were forbidden to publish for ten days. Apart from these three occasions we have never failed to publish on the first day of the month unless that happens to fall on a Sunday when we publish on the last day of the previous month. Acts of war and acts of governments may not come into the same category as acts of God, but we scarcely feel that we can be blamed for delays due to either of these unforeseeable circumstances.

A Strange Tax

EVERY month *The Practitioner* sails to the four corners of the globe enclosed in envelopes (known to the trade as "bags"), designed to withstand rough handling by hands of many colours. These envelopes are made in the Metropolitan Borough of Southwark of "tuff-stuff", a costly paper but the strongest at present obtainable. It is a striking commentary on the strange world in which we live that the purchase tax payable to the Treasury on these envelopes is more than the total pre-war cost. It is perhaps asking too much of a Treasury official to expect him to be able to discriminate between the envelope in which a technical journal is wrapped and that which football pool promoters use, but to the simple medical mind the absence of such discrimination is tantamount to a tax on knowledge. We are not alone in this feeling of resentment as our contemporaries are equally heavily taxed on their wrappers. It is, however, reassuring to notice that many subscribers re-use these envelopes for all manner of purposes, e.g., the doctor's wife who finds it a useful wrapper for sending odd items of clothing to children at school. Unfortunately the second and third users often omit to cross out our address, and so the well-worn envelopes with assorted enclosures are apt to return to Bentinck Street, still serviceable but without their pristine gloss.

THE ETIOLOGICAL PROBLEM OF ACUTE POLIOMYELITIS

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In this article an attempt will be made by a clinician to present some facts regarding acute poliomyelitis; for these we are indebted to research workers, past and present, who have devoted themselves to the study of this disease.

CLINICAL FEATURES

Although it is more than forty years since Wickman drew attention to the existence of healthy carriers and abortive cases of poliomyelitis, the fact that paralysis is an uncommon complication of this infection has been slowly recognized, more especially in countries like England which, until recently, have had little experience of the disease. The proportional incidence of the various forms of poliomyelitis virus infection varies within wide limits. Assuming that the strains of virus causing an epidemic are of average virulence, it is probable that the number of healthy carriers in an infected area is considerable, that abortive cases (minor illness) are the next largest group, and that non-paralytic cases exceed paralytic in a proportion that varies from epidemic to epidemic. It has been estimated (Casey *et al.*, 1946; Howe, 1949) that for every case of paralytic poliomyelitis there are 99 others suffering from an infection with the virus which, in the majority, shows itself by headache and fever with or without catarrhal or intestinal symptoms (abortive form or minor illness). These symptoms pass off in the course of a few days. In a minority of cases such symptoms are accompanied by meningeal signs and changes in the cerebrospinal fluid (non-paralytic form). Recognition of the abortive form of the disease is usually a matter of either inference or speculation, more especially when there is no proof of the more serious forms of the disease in the district. But, in view of the importance of rest in such cases in reducing the likelihood of paralysis, practitioners should regard any unexplained minor illness in a child or young adult, especially during epidemics, as a possible case of poliomyelitis virus infection, and should ensure that such a patient is confined to bed until fever and other symptoms have completely cleared up. Although several viruses and bacteria are known to cause a lymphocytic type of meningitis, it is generally agreed that the virus of poliomyelitis is the usual cause of a benign form of meningitis (non-paralytic poliomyelitis).

At the present time the paralytic form of the disease behaves during epidemics much as it has always done, hitting both the brain-stem and the spinal cord, although the intensity and localization of its attack may vary

according to age, resistance, and the virulence of the virus. The mortality rate continues to vary from 5 to 30 per cent., a higher rate tending to occur in adults. Recent studies on the cerebrospinal fluid have shown that although a pleocytosis and increase of protein occur in the great majority of cases during the acute phase, occasionally the fluid may be normal initially, although a marked rise in the protein figure may occur between the second and fourth week.

PRECIPITATING FACTORS

Little is known of the factors which determine whether or not an infection with the virus of poliomyelitis will result in paralysis. On theoretical grounds an attack of tonsillitis or enteritis might favour the passage of the virus to the nervous system. The fact that in practice there does not appear to be a close association of this sort does not mean that in individual cases one or other of these conditions may not operate in favour of the virus. The following would at times seem to precipitate paralysis:—

(1) *Recent tonsillectomy.*—Here the evidence is clear-cut and suggests that the virus gains access through the traumatized tonsillar bed to the terminal filaments of the 10th nerve, and by ascending them causes a bulbar palsy.

(2) *Physical fatigue.*—Russell (1947) has drawn attention to the effect of physical activity in the pre-paralytic stage of the disease in reducing the resistance of the anterior horn cells to the virus. Although this is true of many cases, there are others in which fatigue plays no part; for example, in 1944, 5 per cent. of paralytic cases in British personnel in the Indian Army occurred in hospital patients who had been undergoing treatment for some other condition for a period exceeding two weeks. No other cases of poliomyelitis were under treatment in these hospitals (McAlpine, 1945).

(3) The factor of *lowered resistance.*—Traditionally the disease is stated to attack persons, especially children, who are in good health, but exceptions to this rule are by no means rare. The example just given, of the disease in hospital patients, suggests that occasionally a lowered state of resistance may play a part. In India a history of dysentery or malaria occurring shortly before an attack of poliomyelitis was relatively common, whilst in a small percentage of cases an inoculation had been shortly followed by paralysis. The state of general health preceding an attack of paralytic poliomyelitis is a subject which would repay further study.

(4) *The rôle of trauma.*—Although trauma is a rare precursor of paralysis due to poliomyelitis virus, it is of interest since it may determine the major site of paralysis (quoted by Lacey, 1949).

ACUTE POLIOMYELITIS AS A WORLD PROBLEM

During the first world war and in the years immediately following it there was no notable increase in the world incidence of the disease. However, from 1930 onwards the virus gained ground, particularly in America, in European countries, in Australia and New Zealand (Bertenius, 1947; Sabin,

1949). During the second world war a virulent form of the disease attacked British and American troops serving in the Middle East, India and Japan; at the same time there was no evidence that the incidence of the disease was at that time any higher in the native populations of these countries. The Malta outbreak of 1942-43 was the first of a series of epidemics that have within the past five years struck island populations, notably Mauritius, St. Helena and Reunion Island. In the East the disease has recently become more apparent among both the native and white populations, for example, in Singapore (Professor G. Ransome, personal communication). In 1949, Bombay experienced its first epidemic. The 1947 epidemic in England was the largest ever experienced by this country, and was followed in 1948 by another of nearly comparable size. Lastly, more cases were reported in America in 1949 than in any previous year (Dr. A. Sabin, personal communication).

AGE INCIDENCE

During the past three decades one of the most striking and puzzling features of acute poliomyelitis has been the rise in the age incidence of the disease in most parts of the world. In certain American cities there has been a continuous decrease in the incidence in the 0-5 age-group, with a maximal incidence in the 5-9 age-group. In the 1944 epidemic in New York the attack rate for the 10-14 age-group was practically identical with that of the younger children (Sabin, 1949). A similar trend was shown during the Australian epidemic of 1937-38 (Burnet, 1940). The epidemic in England in 1947 and the Berlin outbreak of 1947 showed a similar rise in age incidence. Approximately one-third of all paralytic cases in England in 1947 occurred in persons over the age of fifteen (Gale, 1948). For many years it has been recognized that the age incidence of paralytic poliomyelitis is related to living conditions; the higher the density of population and the more primitive the living conditions, the greater will be the tendency to infection in early childhood, thus accounting for the higher rate of paralysis in the 0-5 age-group. That this is true of such countries as Egypt, India and Japan seems highly probable. Burnet (1946) points out that the rise in age incidence has taken place mainly in more highly civilized countries, such as the United States, Canada, Scandinavia, Australia and New Zealand, and that their higher standard of living conditions may tend to diminish the spread of intestinal and respiratory infections, thereby reducing the chances of immunizing subclinical infection with the virus of poliomyelitis in early childhood. Hammon (1949) writes: "If immunity is relatively temporary and the carrier state not prevented, it will be constantly renewed by re-infection, but may wane and lapse where a number of years occur between exposures. Such conditions of waning immunity could be postulated in areas where the greater number of cases is reported as occurring in late childhood and among adults". Sabin (1949), in a study of epidemiological patterns of poliomyelitis in different parts of the world, finds that the occurrence of epidemics, the level of endemic attack rates and age selection patterns are

continually changing, even in countries with advanced sanitation and hygiene. He believes that the principles of latent immunity and the part played by different strains of poliomyelitis virus do not provide a satisfactory explanation for the rise in age incidence. The complexity of the problem is obvious. Inadequate exposure to the viruses of poliomyelitis in childhood would, however, seem to be an important factor.

THE POLIOMYELITIS VIRUSES

Man is the only known reservoir of the virus. Apart from a few special strains which are pathogenic for rodents, the monkey and the chimpanzee are the only animals suitable for experimental work. The viruses of poliomyelitis are potentially neurotropic, but man's natural resistance to them is high; consequently after infection they seldom reach the nervous system in an amount sufficient to cause paralysis.

The proof that several types of poliomyelitis virus exist comes from immunological experiments. Burnet and MacNamara (1931) were the first to demonstrate this fact. Progress has been slow, since the technical problems in these tests, and the difficulty in obtaining a sufficient supply of monkeys, are considerable. However, a great advance was made in 1939 when Armstrong isolated a strain of virus from a case of bulbar palsy which occurred in Lansing, Michigan. He succeeded in adapting this strain from monkeys to rodents, i.e. cotton-rats, and subsequently mice and hamsters. The isolation of this strain and the fact that certain rodents are susceptible to monkey-adapted virus led to the isolation of at least three other strains similar to, but immunologically distinct from, the Lansing strain; these include two strains from the Middle East. Other strains belong to the non-Lansing group and for their detection monkeys are essential for immunological tests. These tests are mainly determined in two ways: (1) by re-infecting monkeys convalescent from experimental poliomyelitis with the same strain and with different strains; (2) by cross-neutralization tests with sera obtained from animals which have been immunized with live or attenuated strains of poliomyelitis virus. The number of non-Lansing strains is at present unknown, but work now proceeding in America should within the next few years clear up the question of the strains which are responsible for epidemics of the disease. Recently a group of viruses has been described which are capable of causing a meningo-encephalitis in mice and occasionally in man (Theiler, 1937; Gard, 1943). Although they show certain features in common with the true poliomyelitis viruses, they are considered by most authorities as being distinct.

Since the behaviour of the virus in the monkey is similar to that in man, much has been learned from the experimental method. Contact of the virus with olfactory nerve endings, brain and peripheral nerves may produce the disease in monkeys, and by these methods the mode of spread of the virus in the nervous system has been studied (Fairbrother and Hurst, 1930; Bodian and Howe, 1940). The monkey can also be infected by feeding the virus by mouth or stomach tube; as a result the nervous system may be invaded with or without signs of paralysis. The virus may be passed in the stool for weeks or months. Neutralizing antibodies may be detected in the serum of monkeys, and also in the pharynx but not in the fæces. Mostly these findings have been paralleled in human beings.

IMMUNITY IN MAN

There are two ways in which active immunity to a virus may be assumed:

(1) by demonstrating the existence in the blood serum of antibodies to the particular strain of virus being tested; (2) from the observation that an individual who has been attacked by the virus is protected from a further attack by that strain. During the Swedish epidemic of 1913, Kling and Levaditi found that the sera of contacts neutralized the virus, and they were the first to infer that immunity was due to latent infection. Using the old M.V. strain of poliomyelitis virus, a number of immunological studies were subsequently carried out in order to detect antibodies to that strain in convalescent cases and healthy persons. In recent years the Lansing strain has been substituted for the M.V. strain in these tests. The following are some facts that have emerged from this work:—

(1) Passive immunity is passed from mother to child (Aycock and Kramer, 1930); it may persist for the first year of life.

(2) From one year upwards, there is a gradual increase in the percentage of individuals showing neutralizing antibodies in the serum (Harmon and Harkins, 1936; Turner, Young and Maxwell, 1945).

(3) The more primitive the living conditions of a populace the earlier in life will antibodies appear (Hammon, 1949; Sabin, 1949).

(4) The Lansing strain and probably other strains of poliomyelitis virus are widespread throughout the world.

Until recently much doubt was thrown on the value of neutralization tests in acute poliomyelitis because there seemed to exist little relationship between the presence of antibodies and a history of previous poliomyelitis infection. Formerly, the theory of maturation was favoured by some workers: this assumed that immunity to poliomyelitis in adult life was a natural phenomenon occurring with increasing age, quite independently of previous infection with the virus. In 1931, Aycock expressed a contrary view: "Immunity occurs only under circumstances in which association with the virus is possible. The development of immunity follows laws of infection and does not follow any law of maturation". He considered that immunity in poliomyelitis varies with the concentration of population in a manner consistent with variations in opportunities for exposure. Recent proof of the existence of several immunologically distinct strains of virus throws new light on the whole question, and has established beyond all doubt the specificity of immunity in this disease.

Morgan, Howe and Bodian (1947), using the intramuscular route, have shown that monkeys vaccinated by four injections of Lansing-infected monkey spinal cord at intervals of one to two weeks, were found to be immune to a massive dose of active virus injected intracerebrally. The same dose produced paralysis in 16 out of 17 normal monkeys. The vaccination method induced a high level of antibody in the serum which was well maintained at the end of a year. Negligible amounts were found in the central nervous system. Further work by the same authors has shown that the degree of immunity increases with an increase in the dose of active virus. If, on the other hand, heterologous virus was used, the previous vaccination did not protect the animals against paralysis.

By carrying out neutralization tests against each patient's own strain of virus within a few days of the onset of the disease and for varying periods

afterwards, Hammon and Roberts (1948) and Steigman and Sabin (1949) have found that antibody is specific and results from a rapid response of the patient to the strain of virus causing the illness. Does a single exposure to a particular strain confer lasting immunity? No definite answer to this question can be given. Aycock (1931) wrote: "If the phenomenon of adult immunity is attributed to the virus, it must be implied that immunity from the initial exposure tends to be permanent or that a more or less temporary immunity is re-enforced by subsequent exposure often enough to obtain the accumulated immunity with increase in age". Aycock favoured the latter view. In a recent survey of this subject, Hammon (1949) gives reasons for the belief that immunity in poliomyelitis is variable, tends to be temporary and is renewed by re-infection. Rare instances of two attacks of paralytic poliomyelitis could be explained on the basis of infection by different strains of virus; however, in the vast majority of paralytic patients immunity is lifelong. The position of non-paralytic cases is not so clear, but may be similar to that of paralytic cases. With these exceptions it seems probable that a single subclinical attack of poliomyelitis virus infection confers only a temporary immunity.

METHODS OF SPREAD

In a monograph published in 1907 in German and translated into English in 1913, Wickman described investigations made during the Swedish epidemic of 1905, which led him to recognize the important part played by healthy carriers and abortive cases in the spread of the disease. He emphasized the frequency with which the disease, often in an abortive form, affected more than one member of a family. The occurrence of the disease in small foci appeared to him to be explicable on the same basis as the spread within a family. He drew attention to the tendency for spread by radiation from a focus. He was also impressed by the intimate association of the disease with main roads, particularly in districts in which cases were scattered either singly or in small groups. After considering such possibilities as infection by food or animals, he concluded that acute poliomyelitis was a contagious disease and that healthy carriers and abortive cases were the principal sources of infection. Confirmation of the truth of Wickman's views has been provided both by subsequent field studies and by experimental bacteriology, notably by Kling and Levaditi, who in 1913 surveyed outbreaks in two islands in the Baltic, and more recently by Casey (1942) and Casey, Fishbein and Bundesen (1945). The latter found that multiple cases of infection in a family were the rule rather than the exception. On the experimental side, the evidence of infection in contacts is equally strong; for example, Langmuir (1942), in a survey of homes within a two mile radius of three affected families, showed by monkey inoculation that the stools of four out of eight adults, and sixteen out of nineteen children, who had been in intimate contact with a case, were found to be positive.

Up till about 1937, infection of the nervous system in man was presumed to take place by the nasal route, as in the experimental monkey. However,

the work of Toomey (1935), of Paul and Trask and their co-workers (1938, 1939, 1940), of Bodian and Howe (1941) and others, has narrowed the portal of entry to the alimentary tract. It has been shown that the virus can be isolated from the pharynx and tonsillar region for three days before the development of symptoms, and for four to five days afterwards, and from the stools for a variable period that may extend to several weeks. The fact that the infectious stage of the disease closely corresponds to the period during which the virus is present in the pharynx and tonsillar region supports the theory of droplet spread. On the other hand the presence of the virus in the fæces for a period that may extend to several weeks, the seasonal incidence of the disease in both northern and southern hemispheres, and the frequent association of epidemics with dry summers such as those of 1947 and 1949 in England, would seem to favour spread by fæcal contamination, either by fingers or through the intermediary of flies.

Several ingenious experiments have been carried out in America in order to prove or disprove the possible rôle of flies as a vector. In one experiment food exposed to flies in homes of poliomyelitis patients became contaminated with the virus and caused the disease in chimpanzees (Ward, Melnick and Horstmann, 1945). Sabin (1947) believes that the high incidence with which the virus is found in flies caught in clean and sanitary urban areas is significant. However, the prolongation of epidemics into winter months, as in England in 1949, and the fact that occasionally epidemics occur in mid-winter, suggest that the fly plays a minor part in the spread of the disease, except possibly at the beginning of an epidemic, as suggested by Sabin. Contamination of food may have accounted for the fact that for four consecutive years during the recent war the incidence of sporadic poliomyelitis in India was five times higher in British officers than in British other ranks (McAlpine, 1945). It seems probable that the methods of transmission of the virus may vary both in the epidemic and sporadic forms of the disease. Pharyngeal secretions may be spread by droplets, and fingers may convey infection from this source as well as from fæces, either by direct contact or through the intermediary of food and fomites. The rôle of the fly as a vector, strong though it may seem to be from experimental work, remains unproven.

Finally, a brief reference must be made to the increasing prevalence of poliomyelitis in various parts of the world. The tendency for the disease to assume a pandemic form was not seen until after the second world war. In seeking an explanation for the recent rise in susceptibility in various communities, due consideration must surely be given to one potential factor, namely the increased contact between the peoples of the Western and Eastern hemispheres due to troop movements and swifter travel, and the possible transference of strains of virus from one country to another.

CONCLUSION

Recent work would suggest that exposure to the viruses of poliomyelitis is inevitable and recurrent in most parts of the world. Owing to man's natural

resistance, paralysis is a comparatively infrequent complication of this infection; therefore the term "poliomyelitis virus infection" would seem preferable to that of acute poliomyelitis. Adequate rest in the early stage of the disease may reduce still further the already small risk of paralysis. These facts should help to allay the anxiety of the public during future epidemics in this country. Since it is probable that subclinical infections with the viruses of poliomyelitis during childhood are necessary for the development of immunity in later life, there seems justification for the recent trend in America towards some relaxation in the preventive measures usually recommended, particularly with regard to the closure of schools. Lastly, the slow progress of research work on poliomyelitis viruses in this country is due solely to the lack of experimental facilities.

I wish to acknowledge the helpful criticism which I have received from Professor F. R. Selbie of the Bland-Sutton Institute of Pathology.

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DISSEMINATED SCLEROSIS

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DISSEMINATED sclerosis was first recognized from the pathological anatomy of specimens examined post mortem. This material had been removed from clinical cases which had become chronic and had died long after the onset of the malady. It is unfortunate that this early work by Cruveilhier in the Salpétrière in 1835, and by Carswell in London in 1838, should have focused subsequent study upon the latest stages of the disease, so that workers upon this subject were led to the erroneous view that the fibrosis (neurogliosis or sclerosis) demonstrated in the patches of the disease were the primary cause, whereas the truth is that the pale gray patches represented attempts at repair and localization of the damage already done. In other words, the "sclerosis" proves to be a secondary effect of the damage done by the "noxa" and is not the primary cause of the whole process.

J. M. Charcot (1868) is generally recognized as the first neurologist to give a complete account of all the features of disseminated sclerosis in its established clinical forms. It must be remembered that in those early days the more recent clinical, biochemical, and neuropathological aids to diagnosis and proof were unknown; therefore many cases of neurosyphilis, virus disease of the nervous system, as well as other lesions of the brain and spinal cord, were included in, or omitted from, the earlier published papers. As reliable statistics are therefore not available it is not possible to assess whether disseminated sclerosis is more common nowadays, in proportion to the number of people living, than it was 100 years ago. Since the advent of modern methods for staining tissues, neuropathology has established new facts in its own scope of observation. Excellent and full accounts of the disease, with its clinical features, are available in many papers, for example, Volume 2 of the "Reports of the Association for Research in Nervous and Mental Diseases (multiple sclerosis) 1922", and the review of disseminated sclerosis by Russell Brain (1930). My own views on the subject will be expressed as personal opinions based upon the study of over 250 cases of disseminated sclerosis. Some of these patients have been under observation intermittently for long periods, during which various methods of treatment have been applied. Some recorded observations, and deductions therefrom, as well as the results of treatment, will be summarized at the end of this article.

INCIDENCE AND ETIOLOGY

Disseminated sclerosis is now the most common organic disease of chronic nature in young people between twenty and thirty-five years of age in this country. In my own cases I find that more young women are affected than young men, in round figures about 6 per cent. more. These figures differ

from American recorded cases and from most European continental figures, which give a slight preponderance to the male sex. All statistics are full of sources of fallacy in that early cases, and cases with long and almost complete remissions, may be overlooked. Among conflicting views it may be stated, as a general truth, that the sexes are almost equally affected, and that familial tendencies and incidence are unimportant. Many published statistical studies upon the alleged predisposition caused by certain occupations, by the effects of toxic substance, or by deficiencies in vitamins, copper salts, and certain foodstuffs, are all without any clear proof, and fail to produce any agreement among experienced observers. In my cases I found that achlorhydria was not more common in disseminated sclerosis than among ordinary medical patients of the same age periods.

The *racial incidence* is more remarkable. Disseminated sclerosis is more common in the northern part of Switzerland, Scandinavia, Germany, Finland and France, than it is in Southern Europe, Turkey or Japan. Among Negroes the disease is uncommon, both in Africa and in the Negro population of the United States of America. In North America the Scandinavian stocks are more often affected; Army statistics proved that native-born members of these families were less often affected than those born in Europe.

Social surroundings, trauma, and prolonged strain, or exposure to wet and cold, all do not seem to play any direct part in etiology; although prolonged exposure, or infections, may play some part in predisposition to, or aggravation of, this malady. In my own cases I have found a large number of patients in whom an "influenza-like" febrile illness has preceded the first symptoms by a week or ten days; in two cases, one the brother of a medical friend, the injection of an autogenous vaccine from nasal mucus was closely followed by the first symptoms of the disease, which subsequently ran its usual course. These experiences are personal ones and are not generally supported by the experience of neurologists with whom I have discussed these findings.

PATHOGENESIS

The general consensus of opinion is that disseminated sclerosis is caused by a "noxa", or filterable virus, which gains access to the nervous system by means of the blood stream, or *via* the perivascular lymphatics. All the earlier experimental work which seemed to prove that some spirochæte or living organism was to blame for the early pink "plaques" described by Nageotte and Riche as "multiple inflammatory foci" has been incapable of proof up to this date. The "plaques" are developed around a blood vessel, and are often large enough to see with the unaided eye, but the cause and origin of this process remains a mystery.

The "deficiency disease" theories have remained quite without proof. Because the essential lesion is a patchy erosion of the fatty myelin sheaths, and the axis cylinder processes and nerve cells are histologically healthy in appearance in the early stages, it has been suggested that some lipolytic

enzyme might be the essential cause of the lesions. These views were put forward by Brickner (1930) but have not been confirmed by other workers. Putnam's view that the myelin degeneration is secondary to thrombosis in small cerebral veins finds no general agreement. It is more likely that the local thrombosis, when it does occur, is itself a secondary process. The patches of disseminated sclerosis are usually numerous around the ventricles in the brain, and in close relation to the Sylvian aqueduct, a fact which has led to much speculation as to a possible entry of an infective agent *via* the cerebrospinal fluid. This theory is unlikely to be true because the spinal fluid obtained by lumbar and cisternal punctures has rarely shown any gross abnormality, even in recent and advancing cases of the disease.

The olfactory mucous membrane with its "undefended space" has always seemed to me to be a likely portal of entry. Certain dyestuffs instilled into the nose can be demonstrated post mortem, as far back as the anterior perforated spot, and on the under-surface of the brain. It is necessary to emphasize that the thin-walled blood vascular and lymphatic vessels are in intimate relationship with the connective tissue spaces in the central nervous system. The blood is circulated throughout the reticulo-endothelial vessels and spaces, which are lined by endothelial cells capable of "filtering off", by vital and chemical actions, waste products of metabolism, and supplying through these intact cellular walls the necessary filtrable gases and other chemical substances necessary for the health of the nervous tissues. These tissues react quickly to any changes in the pressure and chemical composition of the circulating fluids, so that any prolonged departure from the normal ranges of variation is quickly followed by a loss of function, or a variation in the activity of the nervous tissues so affected.

It should be remembered that the living and healthy endothelial cells are also protective in their functions. The intact "filter" of cells will hold back from the relatively defenceless nervous tissue all foreign particles, living organisms and probably other noxious agents of large molecular size. On the other hand, it is most likely that the large molecules of protein "antibody" will also be unable to reach the nervous tissues beyond the reticulo-endothelial walls of the vascular system, and a means of defence be denied to these tissues if ever the "noxa" penetrates the endothelial wall. Some such mechanism may be at work when the "noxa" is able to establish itself beyond the reach of blood-borne antibodies, and therefore continue to damage the nervous tissues in spite of very evident and visible measures of defence on the part of endothelial phagocytes and the neuroglial cells in their efforts to localize the damage. The cellular activities can be seen by suitably stained sections of tissue when viewed through the microscope. Natural remissions may occur if the reticulo-endothelial "filters" are temporarily permeable by local damage, or by some deliberate treatment, such as induced pyrexia or therapeutic malaria. In the same way, as a result of temporary damage, the endothelial and vascular tufts of the glomerulus and Bowman's capsule allow albumin to filter through to the kidney secretion

during pyrexia. This speculation is a personal view, and I believe that some such process would explain the natural and induced remissions so characteristic of disseminated sclerosis in a way better than any other known to me. The speculation seems to harmonize with the morbid histology of the disease, because it will explain the clinical features of the early and later phases without a long and tedious recital of many "clinical types", according to the anatomical sites of the multiple "plaques".

HISTOLOGY OF EARLY LESIONS

At the centre of an early patch of the disease there is usually a blood vessel to be seen; the perivascular distribution around terminal branches and a tendency to spread *via* neighbouring perivascular spaces was fully described by Dawson (1916). Any excess of cells in the "acute" patch is made up of endothelial cells, and the reaction of the local neuroglial cells. The patchy removal of the myelin fatty sheath of the axis cylinder process leaves the neuraxon intact until secondary fibrosis ("sclerosis") interferes with nutrition, and degeneration eventually occurs. The patches are numerous in later stages of the disease and are found placed around the ventricles of the brain, and near the Sylvian aqueduct, although always in close relation to a blood vessel. Clinically it is very uncommon to find cases with a syringomyelic syndrome, or other evidence of patches around the central canal of the spinal cord. The patches tend to attack the lateral and posterior columns.

The patchy demyelination is capable of repair, and if the true cause of the disease were known and removed by treatment, complete cure would be quite likely in the earlier stages of the disease. In some cases spontaneous cures or remissions for long periods do occur. I have seen several cases which have become chronic and non-progressive in old women of sixty-five to seventy-five years of age. These cases are examples of Charcot's classical description of the established disease in its chronic form. In progressive cases new patches appear, and older ones may extend, so that unchecked the disease runs an irregular course to end in ataxic paraplegia with bladder troubles, and finally death from an infected urinary tract, or infected bed sores.

SYMPTOMATOLOGY AND CLINICAL FEATURES

The symptoms arise from interference with the functions of the conducting pathways, and would be expected to arise at the earliest stages from disturbances in the integration of those mechanisms which are placed nearest to the favourite sites of the early plaques of the disease. Although the lesions are disseminated widely throughout the central nervous system, certain symptoms notoriously arise early in the course of the disease, and at once arouse the suspicions of the clinician as to their causation. The diagnosis must rest upon a full neurological examination of all the functions of the nervous system, and its effector apparatus, together with the special senses;

careful consideration of the history of onset, and progress up to the date of the first consultation will tell of apparent "cure" of early symptoms, either spontaneously, or after various treatments, and this is of the greatest importance. No localized symptom can be safely ignored, even though it be seemingly trivial and evanescent. The patient's theories of causation, and the effects of treatment, are apt to be misleading. It is well worth the time spent upon separating the wheat grains of fact from the chaff of conjecture in listening to the patient's story of early symptoms.

(a) *Acute onset.*—A sudden interference with clear vision without apparent cause; "double vision", which is often transient, lasting for a few days only, may be the first symptom to lead a patient to seek advice from an ophthalmic surgeon, or from an optician. In a busy general practice the recital of a seemingly trivial complaint by a young patient, who seems otherwise well but who appears to be highly emotional, is apt to be dismissed abruptly when so many people, obviously more ill, must receive careful attention. The sudden loss of visual acuity in one eye likewise escapes full consideration until other and more dramatic incidents, such as loss of full control of the bladder, occur.

A sudden hemiparesis, or incomplete monoplegia, may usher in the early phases of the disease. A persistent numbness in a limb is much more common than hemiparesis, or gross loss of muscular power. Unlike peripheral neuritis, or herpes zoster (zona) there is rarely any pain or hyperæsthesia. Pain is very rare in disseminated sclerosis except in the latest stages, when troublesome flexor spasms of the legs may torment the sufferer. Loss of sensation to touch and pinprick is rarely found on examination in early cases. Postural appreciation, when the smaller joints are passively moved, is often impaired, especially when the posterior aspects of the cord are affected, and vibration sensation is defective early in cases in which the postero-lateral parts of the cord are involved. Unsteadiness in gait is often an early symptom, and the ataxia is similar to the cerebellar type. A lesion in the posterior spinal columns gives an ataxia of the tabetic type which is apt to be increased when the eyes are closed, or when walking at dusk or in poor light. In these cases Romberg's test is positive. In some cases of acute onset the disease is rapidly progressive, without notable remissions, until all the limbs are ataxic and paraplegia with a rapidly fatal issue ensues in less than two years. These cases are highly resistant to treatment.

(b) *The type with gradual onset and remissions.*—In these cases the onset may be noticed as a feeling of excessive fatigue after games or exercise. It is observed that one leg drags a little, or that one arm or hand becomes awkward in its muscular performance; or that movements are unsteady. Emotional changes are noticed by friends. Spontaneous outbursts of laughter or weeping occur without adequate causes. Usually the patient becomes euphoric (*eutonia sclerotica*) and excessively optimistic as the latest stages, with paraplegia, develop. Gross mental disorder is not common. "Scanning" or syllabic speech and severe ataxia are not usually present until the later

stages of the disease are reached. Double vision, without gross paralysis of the external muscles of the eyes, is common, and often passes off in a remission, to appear later in a period of exacerbation. Long remissions lasting for several years are not uncommon, and may be so complete as to lead to claims of permanent cure. In some elderly patients sent from London hospitals during the war the disease seemed to have become non-progressive, and had remained so for periods of ten to twenty years. When examined they exhibited all those classical features of the disease described by Charcot. These old ladies had many interesting stories to relate as they talked with pride and affection of the opinions and mannerisms of some famous neurologists under whose medical care they had been over a generation ago. These facts are related to emphasize that apparent cures do happen, that long remissions are not uncommon, and that in a few older people the disease apparently ceases to advance towards the paraplegic state. In the chronic stages of the disease the most prominent feature is the spastic paresis of the limbs, owing to the interference with the long pyramidal fibres from the motor cortex down the length of the spinal cord. The ataxia is chiefly due to incoordination of the muscles but is often made more disabling by damage to the cerebellar apparatus and the long sensory pathways in the posterior part of the spinal cord, i.e. postural sensibility.

In disseminated sclerosis it is the rule to find gross spastic paresis with little demonstrable loss in skin sensibility: a valuable diagnostic point.

DIAGNOSIS

Owing to the scattered distribution of the "plaques" the disease may present a complex series of symptoms which alter during months, or years, with remission and exacerbation so characteristic of the malady. In a case of several months' standing this story of recession and worsening is almost diagnostic. I have already considered many of the symptoms and will now turn to physical signs.

(a) *Cerebral functions* are usually unaffected except for the lack of control of the emotions, and the optimistic outlook which fortunately helps both the sufferer and all those whose task it is to help the patient and treat the disease. The hemiplegic type simulates the early ravages of a glioma cerebri, or a vascular lesion, although both these lesions cause more complete damage than disseminated sclerosis. The clinical features of embolic lesions from bronchiectasis, or valvular heart disease, make these incidents simple to distinguish from disseminated sclerosis.

(b) *Cranial nerves.*—In those cases with eye symptoms it is exceedingly rare to find papillœdema. Blindness in both eyes with papillœdema and myelitis of the transverse type I have seen only twice in thirty-seven years; and both cases were neuromyelitis optica (one case verified post mortem) and not disseminated sclerosis. One eye is usually affected in disseminated sclerosis, and the common ophthalmoscopic findings, very early in the

disease, i.e. exaggerated pallor of the outer parts of the optic discs, are usually more marked in one eye. Colour vision to red and green is often slightly defective early in the disease. Pathological pallor of the optic discs was noted in approximately 56 per cent. of my cases at the first visit. The pupils are rarely abnormal, except when optic atrophy will explain a defective reaction in the light reflex of the affected eye.

Diplopia is common, and occurs in about 30 to 35 per cent. of all cases. Rarely is it possible to demonstrate a gross paralysis of the individual external eye muscles. The ciliary muscle is affected sometimes and this causes visual defect.

Nystagmus.—In my cases only 46 per cent. have had oscillations which were marked enough to designate as nystagmus. Many writers have put the incidence of nystagmus as high as 70 per cent. or more.

Fifth nerve.—A few cases show a subjective "numbness" on the side of the face, but very little defect is found after careful testing and the symptom may soon clear up.

Facial nerve.—Any weakness of the facial muscles is of the upper neurone type, incomplete, and usually subsides. Affections of other cranial nerves are rare. Syllabic speech is usually a late manifestation of the disease.

The arms.—Transient monoplegia with slight increase in tone and tendon jerks is common; so is a slight ataxia. I find it easier to appreciate slight changes in muscular tone by making rapid pronation and supination movements of the forearm passively while the patient relaxes the arm and the observer holds the elbow flexed. The Rossolimo (1905) type of tendon reflex is not reliable for diagnosis in early cases. This reflex is a proprioceptic type of reflex due to tendon stretching. Hoffmann's sign is verifiable after an epileptic convulsion when the muscles are relaxed, and therefore it cannot be due to spasticity alone. This reflex is more often positive in cases of lesions at or near the motor cortex than in interference at cord level.

Abdominal reflexes.—These skin, or superficial, reflexes are most reliable guides when an attempt is being made to diagnose a lesion of the pyramidal fibres in young people. Perfect relaxation, a warm skin, and the absence of local lesions or abdominal disease are essential for a reliable test. In my cases the abdominal reflexes were absent or defective on one side or the other in 84 per cent. of all cases. For purposes of early diagnosis I consider this test superior to a doubtful plantar skin reflex.

The lower limbs.—Early motor changes in one or both legs are noted, usually with increased tone, exaggerated tendon jerks, with knee and ankle clonus. Ataxia is commonly an early symptom, confirmed by clinical testing. An interesting and reliable tendon stretch reflex was described by Gonda (1945). It is elicited by the slight pinching and sharp downward flexion of the 3rd or 4th toe, pressing on the pulp of the toe. The movements and significance are the same as for the Babinski phenomenon.

Plantar reflexes.—After the early stages it is almost invariable to find extensor plantar reflexes and a full Babinski phenomenon when the feet are

tested warm, and the outer side of the sole scraped with a wooden match stalk. This clinical weapon is desirable because it can be broken off, and the deposit of insanitary epidermis discarded with it.

Organic reflexes.—Micturition may be precipitate in both sexes in the early stages of the disease, and incontinence of urine is occasionally an incident which leads a patient to seek advice. There is no pain, and the symptom is worth a full neurological examination, even in women who have borne children and in whom a suspected local cause may explain the occurrence. Incontinence of fæces is rare, but obstinate constipation is common both in disseminated sclerosis and in tabes doralis. Incidentally, a useful remedy is a mixture of cascara, glycerin, and tincture of hyoscyamus.

Lumbar puncture.—The cerebrospinal fluid rarely gives diagnostic aid of much value, although a clear fluid with few lymphocytes, a negative Wassermann reaction and a "paretic" curve with the Lange colloidal gold suspension are confirmatory of the clinical findings. In doubtful paraplegic cases the cerebrospinal fluid is of great value in diagnosis. The absence of a rise in the pressure when pressure is made on the veins in the neck, and a high protein content in the fluid, would all be in favour of compression paraplegia, and against disseminated sclerosis.

DIFFERENTIAL DIAGNOSIS FROM ACUTE DEMYELINATION DUE TO OTHER DISEASE

The question whether acute disseminated encephalomyelitis is a fulminating type of disseminated sclerosis, or is really a separate disease, is a research problem into a rare disease. The course and clinical features of these diseases, e.g. Schilder's disease, neuromyelitis optica, are unlike disseminated sclerosis, and are so rare that we need not deal with them in detail. Of much more interest is the recently revived suspicion that certain virus diseases in cattle, e.g. "swayback" and "staggers" in sheep, may affect men, in whom the virus produces an entirely different clinical picture. "Staggers" in sheep results from an acute destruction of cerebellar cells by virus which produces in man a syndrome very like that of tuberculous meningitis, except that the patient spontaneously recovers, and the bacillus of tuberculosis is not to blame. I have seen two such cases of "louping ill", one of which began with diplopia in a young woman, so that we first suspected disseminated sclerosis.

Neurosyphilis, so common thirty years ago, is much less evident in hospital practice to-day. The pupillary changes, different clinical features, and positive serum and cerebrospinal fluid reactions make differential diagnosis easy in these days.

TREATMENT

No specific remedy is known. The lack of exact knowledge of the causation of this disease is a great handicap when one attempts to influence its course. My personal view is that all vaunted treatments which have been found of some use have only one common factor, i.e., they upset the patient tem-

porarily, and often cause pyrexia when given in full doses. Some therapeutic agents, such as malarial infection, raising the body temperature by intravenous injections of typhoid vaccine, by radiant heat or diathermy—all aim quite deliberately at artificial pyrexia. The "direct actionists" inject substances directly into the spinal meninges by lumbar puncture. Like many other workers in this field I have tried sterilized solutions of lecithin, salvarsanized serum, the patient's own serum, mercurialized serum, and many other substances. Intravenous arsphenamine, of which sulpharsphenamine is the most toxic and yet best in action, is often employed, a survival from the time when spirochætes were thought to be the causal agent. Intramuscular injections of bismuth iodate and quinine, and other substances, all have their advocates, but little permanent success can be claimed by anyone. My own view, which is not proved by any means, is that when drastic remedies are given they may upset the liver and the reticulo-endothelial system, so that chemicals or antibodies are able to pass through the vascular spaces and attack some entrenched "noxa" in the nervous tissue.

In many cases in which the disease has been advancing, remissions have followed closely and dramatically on drastic treatment based upon this theory; too frequently to be mere coincidence. The non-remitting paraplegic type of the disease does not respond to such treatment. I have used massive does of penicillin both alone, by intramuscular injection, and combined with pyretotherapy induced by T.A.B. vaccine injected intravenously, without finding any evidence of penicillin in the cerebrospinal fluid withdrawn at the height of the pyrexia, or in apyrexial periods. Clinical improvement has not followed this treatment in the few cases when patients had requested a trial of this remedy. One patient died of hyperpyrexia during the treatment, in spite of nursing care.

Treatment by Frænkel's exercises, massage, hot brine baths, and all physiotherapeutic measures give general help and encouragement to the patients. Electrotherapy is not desirable, apart from diathermy, because it seems to encourage contractures. Much has been done, yet much remains to be done, before any of us can feel satisfied with our knowledge of the cause and treatment of disseminated sclerosis.

This summary would not be complete without an expression of my gratitude and thanks to my colleagues at the General Infirmary at Leeds, to my Registrar, Dr. William Robinson, and to my house physicians, for their kindness and help at all times.

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THE MUSCULAR DYSTROPHIES (MYOPATHIES)

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"The disease is one of the most interesting, and at the same time most sad, of all those with which we have to deal; interesting on account of its peculiar features and mysterious nature; sad on account of our powerlessness to influence its course, except in a very slight degree, and on account of the conditions in which it occurs. It is a disease of early life and of early growth. Manifesting itself commonly at the transition from infancy to childhood, it developes with the child's development, grows with his growth—so that every increase in stature means an increase in weakness, and each year takes him a step further on the road to a helpless infirmity, and in most cases to an early and inevitable death".—Sir William Gowers, "Clinical Lecture on Pseudo-hypertrophic muscular Paralysis". 1879.

PERHAPS because the myopathies have been accepted and then neglected; possibly because of the intrinsic difficulties of the problem, the state of our knowledge remains not very different from that expressed so ably by Gowers in the above paragraph, written 70 years ago. Inevitable and intractable, the myopathies remain subjects of mild interest, lying on the fringes of neurology and of locomotory disorder, more often encountered as short cases in clinical examinations than as objects of scientific study. Despite a few half-hearted attempts at biochemical investigations, and at therapeutic ventures, we are still completely ignorant as to the causation, nature and methods of control in these affections.

HISTORY

The name of Guillaume Benjamin Amant Duchenne (1806-75) is the one most often associated with early knowledge of the subject. A century ago the muscular dystrophies as we know them to-day were commonly confused with the progressive muscular atrophies. In 1852, Duchenne referred to a familial type of progressive muscular wasting often starting in the orbicularis oris. He continued to discuss this subject in later papers, and in 1868 he wrote a study upon "La paralysie musculaire pseudo-hypertrophique"—which he also spoke of as "paralysie myosclérique".

But Duchenne was not really the pioneer, for in 1852 the condition had already been described by that interesting medical figure Dr. Charles Lewis Meryon, the peripatetic physician to Lady Hester Stanhope. Meryon's cases were also published privately seven years later in a pamphlet circulated by the Rev. Lord Sidney Osborne, the vicar of Durweston in Dorset. But even Meryon had been anticipated in his description of the pseudo-hypertrophic type of the disease, by Partridge in 1847, and by Sir Charles Bell, who in 1830 mentioned in his "Nervous System" the following case:—

"A boy, at eight years of age, who began to experience difficulty in rising from a

chair. The disease gradually progressed till at eighteen he had to twist and jerk his body about to get upright. The muscles of the lower extremities, hips, and abdomen were debilitated and wasted. The extensor quadriceps femoris on both sides wasted, but the vasti externi had not suffered so much; a firm body, remarkably prominent, just above the knee-joint, marked the position of the vastus externus. No defect of sensibility or affection of the sphincters. The upper part of the body, shoulders, and arms were strong".

CLASSIFICATION OF THE MYOPATHIES

In 1910, Batten proposed the following classification:—(1) The simple atrophic type (myotonia congenita or amyotonia congenita). (2) The pseudo-hypertrophic type. (3) The juvenile type (Erb). (4) The facio-scapulo-humeral type (Landouzy and Déjerine). (5) The distal type (Gowers). (6) The myotonia atrophica type. (7) Mixed and transitional cases.

(1) ***The simple atrophic type*** was originally described by Batten himself. It differs from all the other types in that it appears at birth or very shortly afterwards. Most commonly the patient is regarded at an early age as suffering either from Werdnig-Hoffmann's spinal atrophic paralysis, or else from Oppenheim's disease (amyotonia congenita). Indeed it was, and still is, a matter of discussion to what extent these three conditions are distinct nosological affections. Aldren Turner has recently shown that in some cases at any rate the early picture of an amyotonia congenita may in adolescence change to that of a simple, but non-progressive, muscular dystrophy.

Batten's types (2), (3), and (4), constitute the well-recognized groups, confidently described in textbooks as separate, although related, entities. It is perhaps insufficiently realized that it is often not possible to distinguish clearly between these three clinical pictures, and that one group may merge into another. Or signs regarded as peculiar to, say, group 2, may also be found in cases belonging to the third and fourth groups. In other words, the more closely the patients are studied, the greater is the tendency to utilize the seventh category of miscellaneous or transitional types.

Gowers' "distal" type must be regarded as a great rarity, if indeed it exists at all, as some would doubt. Probably Gowers, like Spiller before him, was including some cases which would be recognized to-day as belonging either to the "myotonia atrophica type" (no. 6) or else to the disorder better known as peroneal muscular atrophy (or Charcot-Marie-Tooth's disease).

The sixth category isolated by Batten under the term ***myotonia atrophica*** is to-day almost universally spoken of under the title proposed by Curschmann, as "dystrophia myotonia". Here again there is a rich polymorphism and it is still debatable how far this disease is related to the rarer conditions of Thomsen's disease (myotonia congenita), Eulenburg's disease, and myotonia acquisita.

Batten's classification is not altogether satisfactory or comprehensive. He specifically excluded the "secondary myopathy" forming part of the clinical picture of peroneal muscular atrophy; but perhaps he was well advised in this omission, and he may well have been correct in ascribing all of the muscular wasting to a myelopathy. There was no mention, however, of that

curious affection "dystrophia hypertrophica vera" described by Spiller, with its possible variants of true and spurious hypertrophy. Neither did Batten discuss the "late" forms of myopathy, afterwards studied by Nevin; nor those not uncommon types of muscular dystrophy in which the affection starts in the pelvic girdle. The problem of myopathic-like wasting as a complication of thyrotoxicosis, and of the rare association of muscular wasting with myasthenia gravis, finds no place in Batten's monograph.

CLINICAL VARIABILITY (POLYMORPHISM)

The rare studies of large family groups of muscular dystrophy have afforded opportunities for witnessing the variability of the clinical pattern from one affected member to another. One of the most interesting of these groups was described by Diehl, Hansen and von Ubisch; here they could identify three types of individual: the healthy, the myopathic, and the "Typ". The last-named batch was made up of individuals of pyknic habitus with curiously sloping shoulders. Most interesting of all is the remarkable Midland "S" family so carefully recorded by Stanley Barnes.

Starting with an ancestor who was born in 1749—nicknamed "Ducky" on account of his short legs—the family grew to include about 500 descendants of whom at least 160 were personally studied. Many were myopathic. In these the clinical picture varied somewhat. Some of the victims possessed exceptional physical prowess in their pre-morbid period, dystrophic symptoms not developing until between the ages of thirty-five to fifty. Thus Barnes's case 12, in his youth performed feats requiring abnormal strength. He developed myopathy at the age of forty-five and died at seventy. Case 15, known as "Hit-away Harry" was a boxer of Herculean strength and endurance. He too became weak in his legs at the age of forty, although he survived until the age of seventy. Case 46—a furniture remover who could carry a piano on his back—could snap a piece of string tied around his upper arm merely by contracting his biceps; he began to develop a myopathy at the age of fifty. Case 89 used to exhibit feats of prowess, such as raising a 56 lb. weight between the thumb and finger of each hand, or climbing stairs carrying a 500 lb. sack of corn on his shoulders. This man developed symptoms at the age of forty-two. In Barnes's cases, four stages could be recognized: hypertrophic, pseudo-hypertrophic, atrophic, and terminal. In this last phase the muscular wasting spread to involve the hands. As in the case of so many other myopaths, adiposity developed in the later stages.

It is interesting to realize that cases of muscular dystrophy of all types show a tendency to be associated with anomalous features, congenital or acquired, in other tissues, whether ectodermal or mesoblastic. Such associations can scarcely be regarded as coincidental. Thus we should take cognisance of such coexisting conditions as macroglossia (Gowers); ichthyosis, or scleroderma; optic atrophy; the Marcus Gunn phenomenon; mental retardation; Mikulicz's disease; heredo-cerebellar ataxia.

THE VEXED QUESTION OF CONTRACTURES

In this country it is usually taught that the atrophic muscles tend to shorten and to produce deformities, especially when the myopathic patient is bedridden or immobilized. Thus Walshe in his textbook writes that "in the final stage the muscles undergo a fibrous change, shorten, and thus lead to

the development of skeletal deformities and contractures of the limbs". Wartenburg has hotly contested the accuracy of this opinion, and asseverates that "muscular contracture occurs in dystrophy not only very late but very rarely". He quotes Bing as supporting evidence, and also the fact that Cestan and Lejonne drew attention to the peculiarity of their two patients who had contractures and deformities; and to the fact that Steinert even separated a special form of myopathy which he called "dystrophia musculorum progressiva retrahens".

Truth probably lies somewhere between these extreme views. That shortening of the tendo achillis occurs in cases of pseudo-hypertrophic muscular dystrophy and at an early stage, seems incontrovertible. This feature was noted by Meryon in 1859, by Duchenne in 1868, and was well described in Gowers' classical monograph in 1879. Wartenburg is, of course, correct when he restates the orthodox view that the lordosis of myopaths is due to weakness of the extensors of the hip, but it is probable that he has misinterpreted Walshe upon this point.

VULNERABILITY OF CERTAIN MUSCLE GROUPS

It is interesting to speculate why certain muscle groups (or portions of certain muscles) are commonly affected in the dystrophies whilst others usually escape. Of the affected muscles, some begin to waste from the start; others undergo a condition of lipomatous pseudo-hypertrophy: why this should be the case, is not known. Gowers (1879) drew attention to the fact that the latissimus dorsi and the sternal part of the pectoralis major are characteristically affected, whilst the clavicular portion of the latter muscle is spared. According to Gowers, "these muscles are, be it noted, associated in action as depressors of the raised arm, and are perhaps of all muscles of the limbs, *the lowest in physiological importance*". In 1925, Edwin Bramwell elaborated this idea in a most interesting fashion, basing his arguments upon a foundation of comparative anatomy and of embryology. He stressed that in myopathies there is a constant involvement of muscles of three classes:—

(1) ***Those which develop early in the fœtus:*** e.g., the brachioradialis, the extrinsic muscles of the shoulders (serratus magnus, latissimus dorsi, rhomboids, adductor part of the trapezius), and the orbicularis palpebrarum.

(2) ***Those muscles which are regressive*** (in the sense that they no longer fulfil such an important function as in an early stage of evolution) as opposed to those which have been acquired at a later date or which have taken on new functions. Thus the clavicular part of the pectoralis, which is spared, is a new muscle in the vertebrate scale. Again, the sternomastoid and upper trapezius (which also escape) are muscles which have taken on new functions with the assumption of the erect posture.

(3) ***Those muscles essentially associated with the function of fixation, or of the maintenance of posture,*** as contrasted with those concerned chiefly with the more precise movements of grasping and running.

FITS AND THEIR DIFFERENTIAL DIAGNOSIS

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In recent decades various new methods of investigation have been developed for the study of fits, but although these advances are of great interest, their clinical value is limited, and their introduction has caused some confusion to the medical practitioner.

FITS WITH LOSS OF CONSCIOUSNESS

Any kind of attack, fit, blackout or giddy attack which is associated even for a few moments with loss of consciousness or loss of awareness of surroundings must indicate some disturbance of brain function. Apart from hysterical coma, which is easily recognized and will be referred to later, there are two chief causes of sudden loss of consciousness. The first is cerebral anæmia, and the second is an abnormal and disordered activity of the brain cells of the type which in its florid form causes a major epileptic fit.

FAINTS DUE TO CEREBRAL ANÆMIA

The common postural syncope causes many diagnostic errors owing to the frequent failure of the patient to describe his actual sensations, and to his preference for terms such as "I come over giddy", "things go round", which mislead the doctor into thinking of vertigo or a vertiginous aura to a fit. Careful questioning elicits the fact that the patient's warning of an attack of postural syncope is generally visual—things go black, and if he does not sit down quickly he may fall unconscious. Young adults are most prone to these attacks, which generally occur while standing up and relaxed (e.g. standing on parade), or on getting up quickly from bed or a chair. There is generally no convulsion, and the attack can be arrested promptly if the patient learns to lower his head or to brace the abdominal muscles. Plenty of fresh air and exercise usually provide an easy cure. The loss of consciousness while banking in high-speed flying is also due to cerebral anæmia.

There are two other types of cerebral anæmia with loss of consciousness which may be mentioned: the first is in the Stokes-Adams seizure of heart block which may proceed to a convulsion. The second affects old people who drop asleep in a chair after lunch: attacks of pallor and muscular twitching followed by mental confusion may then occur, apparently as a result of cerebral anæmia. Such patients should avoid falling asleep in a sitting position.

It should, of course, be realized that if a vasomotor faint causes a fall and a head injury, the resulting concussion may prolong unconsciousness and

confuse the diagnosis. It must also be admitted that young adults liable to vasomotor faints sometimes also develop a tendency to epileptic attacks.

FITS DUE TO ABNORMAL NEURONAL DISCHARGES (EPILEPTIC ATTACKS)

One of the most mysterious properties of normal brain cells is their tendency, in certain circumstances, to develop bursts of uncontrolled activity which result in an epileptic fit. Every brain can be made to discharge in this way by a variety of physical or chemical irritants. We are all therefore potential epileptics, but in most individuals epileptic fits do not occur spontaneously, whereas in others they occur without apparent cause, and seriously disturb the patient's life. The brain of the epileptic seems to be structurally identical with that of the non-epileptic, but for some reason, which is not understood, his threshold for the occurrence of this discharge phenomenon is lower than it is for the average person. It is therefore preferable to consider epilepsy not as a disease, but merely as a state of altered threshold which may be inborn, or may depend upon some previous damage to, or disease of, the brain.

Petit mal and *grand mal*.—True *petit mal* generally begins in childhood, as an inborn abnormality. The electro-encephalogram (E.E.G.) shows the wave and spike complex, especially on overbreathing. The attacks generally cause a momentary cessation of consciousness, but usually no fall, although there may be slight muscular spasms. Recovery after the attack is as quick as the attack itself, and mental confusion does not ensue even when these minor fits are frequent. Occasionally hysterical behaviour may follow a *petit mal* attack, and this may cause diagnostic difficulty. Focal brain disease is only rarely a cause of true *petit mal*.

Fits which cause sudden loss of consciousness with falling followed by some confusion should generally be classified as *grand mal*, irrespective of there being convulsions. Fits beginning with focal manifestations such as a spasm of one hand spreading over the body (Jacksonian epilepsy) should also be classed as *grand mal*.

DIAGNOSIS

The diagnosis of the nature of a fit depends first upon the patient's description of any aura or other prodromata, and any sensations he experienced during or after the attack. If the patient lost consciousness, then a witness of the fit must be questioned or sent a "fit form" for completion (fig. 1). This is an essential part of the investigation, and should never be neglected.

The circumstances in which an isolated fit occurs are of great importance. An infant may have a convulsion when febrile, or a young adult may have a fit while hungry, and when blood sugar is low. In young people it is sometimes merely meddlesome to carry out complicated investigations such as

REPORT BY WITNESS ON A CASE OF SUSPECTED FITS OR FAINTS

1. Name .....
   Time and date of attack

2. What was the patient doing immediately before the attack occurred?
   Was he standing, sitting or lying down?
   Was he excited, upset or calm?
   What was the first abnormality noticed?

3. Give a general description of the attack

4. In addition to the general description given above, the following questions should be answered if possible:—
   (a) Onset sudden or gradual? Did he fall? Did he injure himself? Did he make a noise or cry out?
   (b) Did he appear to lose consciousness, e.g. could he be roused by shouting or pinching? Did he blink when his eye was lightly touched?
   If unconscious, for how long?
   (c) Colour of face, e.g., pale, flushed, blue or natural
   (d) Eyes open or shut? If shut, could eyelids be opened by the observer?
   (e) Did the limbs become stiff or remain loose?
   (f) Did any movements of the body occur? If so, describe them and their duration
   (g) Was the tongue bitten or was the saliva coloured with blood?
   (h) Was there incontinence of urine or fæces?
   (i) Pulse
   (j) Condition after the attack, e.g., headache, vomiting, confusion, sleep, peculiar or automatic, crying or other emotional disturbances

5. Further observations and opinion regarding nature of attack (continue overleaf if necessary)

6. Name of witness on whose observations this account is based

Date and Time..... Signed .....

M.O.'s Comment

Fig. 1.—Form to be filled in by witness of a fit.

air encephalography, or to prescribe prolonged sedative treatment, after an isolated fit. The practitioner must, however, give instructions which will restrict the patient's activities to those which are safe should another fit occur, and must look for possible evidence of infections or other systemic diseases.

Electro-encephalography.—The electro-encephalographic record has almost become a routine part of the investigation in cases of fits. Its value in diagnosis has, however, been greatly overemphasized, for it rarely gives an unequivocal answer except when the correct diagnosis is already apparent. The accurate diagnosis of fits with loss of consciousness should depend upon the observed nature of the attack, irrespective of the E.E.G. findings. It is clearly of great importance to observe the abnormal E.E.G. record in certain cases of epilepsy, but the diagnosis of the nature of a fit which is past can never depend upon an electrical record taken later. Nothing can replace the witnessed account of what happened.

Workers with the electro-encephalogram are, however, developing improved methods for locating the site of origin of abnormal discharges in the brain, and for the early recognition of organic brain disease.

Family and personal history.—A tendency to cerebral dysrhythmia in the electro-encephalographic sense is found more often in the relations of epileptics than in other people. Some epileptics also exhibit an aggressive "epileptic personality". The personal and familial traits must not, however, be given importance in the diagnosis of a fit. The features of the fit must be assessed irrespective of the personal or family background. *The influence of the patient's personality on the doctor's diagnostic judgment is a frequent cause of serious error.*

Provocative tests.—Various tests have been used which attempt to provoke fits as a diagnostic measure. The pituitrin test is the best known, and the threshold for a convulsion after cardiazol has also been used. These tests are of very limited value, as they merely give some indication of the threshold for drugs which can cause convulsions, and conclusions based on a positive test may not always be justified.

FITS AND ORGANIC DISEASE

The possibility that a fit may be the earliest symptom of organic disease of the brain must always be kept in mind. In children, for example, a fit may be the presenting symptom of meningitis or of those curious vascular lesions of the brain which are now generally considered to be due to cortical thrombophlebitis caused by a spread of infection from the nose or throat. In this latter type of case, there is often some other evidence of brain involvement, such as hemiparesis or hemianopia. Further, cerebral thrombophlebitis in childhood is an important cause of a chronic tendency to fits in later life—often of a somewhat focal nature with perhaps an aura affecting

one limb. A varying degree of "infantile hemiplegia" may be caused by such a lesion, and even if the weakness recovers, some hemi-smallness often persists, which is unnoticed by the patient, but provides the physician with a permanent clue as to the likely cause of focal fits should they appear in later life.

These cases must generally be dealt with symptomatically: surgery is rarely helpful in this type of case. In the middle-aged patient, however, the onset of fits without obvious cause demands full neurological investigation, as the possibility of organic brain disease, such as cerebral tumour, has to be considered first in this type of case.

Focal fits (*Jacksonian epilepsy*).—Fits which have an aura indicating the region of the brain which is discharging first—before loss of consciousness—are now generally referred to as focal fits or fits with a focal aura. The nature of such an aura often indicates accurately the site of beginning brain discharge, and is of great localizing value to the surgeon should he suspect a cerebral tumour, scar or other disease requiring operative treatment. For example, an aura of flashing lights in the left visual field indicates with some certainty a discharge originating in the right occipital lobe. Elaborate visual or auditory hallucinations occasionally occur as an epileptic aura and provide a fascinating glimpse of some of the higher cerebral functions.

Status epilepticus.—When major fits occur in rapid succession the grave dangers of *status epilepticus* must be kept in mind. Every hour this condition is allowed to continue reduces the likelihood of survival, so the fits must be stopped promptly by giving adequate sedative or anæsthetic treatment.

Vertigo, blackouts.—Labyrinthine vertigo may be so sudden as to throw the patient to the ground, but consciousness is usually fully retained, and the patient gives a vivid description of a feeling of violent movement either of himself or of the things he looks at. It should be noted, however, that patients may use misleading terms, such as "everything goes round" for any kind of faint. Vertigo may also occasionally be the aura to a major fit.

Blackouts of the kind which may occur as a post-concussional symptom are often a mixture of postural syncope, mild vertigo on head movement, and blurring of vision due to accommodation fatigue or defect of ocular balance. Consciousness is seldom disturbed, but symptoms of anxiety often complicate the clinical picture: treatment by graduated exercises is often curative.

Some attacks of migraine may resemble a form of focal fit when, for instance, the severe frontal pain is preceded by hemiparesis or aphasia. In such a case, however, the focal symptoms disappear as or before the headache appears.

There is a curious type of blackout in which vision disappears for perhaps a minute—the cause of this is presumably vascular, but is not really known.

PSYCHOLOGICAL FACTORS

In some epileptics, psychological factors appear to precipitate convulsions, and although an epileptic convulsion cannot possibly be a psychological phenomenon, the possible part that can be played by the mind in influencing abnormal cortical rhythms is not fully understood. Hysterical fits and coma, on the other hand, are psychologically determined and generally represent an attempt to evade an awkward situation or to attract attention. Hysterical fits are recognized by their general characters. The eyes are closed and resist opening; the clonic convulsions of epilepsy can seldom be simulated, and the hysterical attack goes on too long to be genuine *grand mal*. A painful stimulus will often arrest an hysterical fit. Appropriate remarks made by the doctor in the patient's hearing will often hasten recovery, for although apparently unconscious the hysteric hears and understands what is said. Difficulty does, however, sometimes arise if a minor epileptic fit is followed by hysterical behaviour, and such a case may require careful observation.

CONCLUSION

The correct diagnosis of fits of all kinds depends largely upon collecting information as to what the patient actually feels before, during and after the fit; and what witnesses observe during the fit. In this connexion the layman's use of terms to describe his symptoms is usually highly misleading, and he must be cross-examined as to what he means by every term used.

Although treatment is not considered here, it must be emphasized that, in the absence of organic disease, all sufferers from fits should, if possible, be kept in regular employment of some kind. Resting the brain or body is of no value in this type of case, and indeed is generally harmful.

Owing to the social and employment handicaps for the epileptic, the label *epilepsy* should not be used without consideration of the consequences. The Army diagnosis of *Convulsion N.Y.D.*, or *Syncope ? cause*, provide convenient temporary expedients.

SCIATICA: ETIOLOGY AND TREATMENT

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In past years the term sciatica was commonly applied to almost any pain arising in the lower extremity, and until the beginning of the present century an acute inflammatory process in the sciatic nerve was regarded as the principal etiological factor (Gowers and Taylor, 1899). Bruce (1903) was the first to have doubts of the existence of sciatic neuritis, and in the following thirty years many alternative theories were put forward. Disease of the sacro-iliac joints was regarded as a prominent cause (Goldthwait and Osgood, 1905; Smith-Petersen and Rogers, 1926; Yeoman, 1928); more recently Bankart (1942) stated that spinal arthritis was the most common cause of sciatica. Hurst (1943) considered many cases to have a psychoneurotic basis. In 1934, Mixter and Barr drew attention to the relationship of intervertebral disc protrusions to sciatic pain, and since that time much has been learnt of the causation and treatment of sciatica.

ETIOLOGY AND DIAGNOSIS

The term sciatica is used here in the generally accepted sense of pain felt in the course of the sciatic nerve. For the most part this bears little relation to the cutaneous distribution of the nerve, although most of the deeper structures in its course derive their nerve supply from it. It is important, however, to realize that interference with the sciatic nerve or its constituent roots will cause pain in the cutaneous distribution of the nerve, and that pain confined to the buttock and back of the thigh can, and often does, arise independently of any process affecting the nerve.

Sciatica in general is a condition affecting males rather more often than females, and is most commonly encountered in the third and fourth decades. Cases fall into three main etiological groups:—

(1) Sciatica due to intervertebral disc protrusion.

(2) Sciatica due to inflammation of muscular and fascial structures.

(3) Symptomatic sciatica due to involvement of the nerve or its roots by gross disease or abnormality of surrounding structures.

SCIATICA DUE TO DISC PROTRUSION

The relative frequency of this condition in the production of sciatic pain is still the subject of differing opinions: Elliott (1942) made this diagnosis in only two of eighty-four patients; Price (1942) made and operatively confirmed the diagnosis in seventeen of thirty patients; Pennybacker (1940) and Dandy (1943) regarded disc protrusions as responsible for the great majority

of cases of sciatica, and Kendall (1947) made this diagnosis in fifty-three per cent. of 305 patients.

In order clearly to visualize the mechanism by which an intervertebral disc may be damaged, some reference to the anatomy of the lower lumbar spine must be made. The lumbar spine is the site of the second of the two secondary curves resulting from the adoption of the erect posture. As a result of this curve the plane of the lower lumbar intervertebral discs tends to slant forward, and the weight of the body acting from above imparts a forward "shearing" strain upon the discs and the ligaments attached to them, in addition to the direct downward force which tends to squeeze out the disc. The lower lumbar discs, and in particular the last two, are therefore dependent largely upon their ligamentous attachments for the maintenance of their correct position between the vertebral bodies. In flexion of the spine the posterior surfaces of the vertebral bodies are separated, and the posterior common ligament which is attached to them and to the annulus of the intervening discs is stretched; thus it is clear that any sudden strain applied to the spinal column in flexion may damage the ligament and its attachment to the disc, whereupon the weight of the body may in time force a part of the disc to protrude between the margins of the vertebral bodies posteriorly. It is in this way that the majority of lumbar disc protrusions are thought to occur, and it is a very characteristic feature that the first symptoms follow some abnormal effort or strain with the spine in flexion, such as lifting a heavy weight from an awkward position or starting a motor car by hand.

Symptoms.—The symptoms associated with disc protrusion occur in two distinct phases: an initial phase of pain in the lumbar region which usually follows closely upon trauma or strain but may be so delayed as to appear independent of injury, and a later phase in which pain is felt in the leg and foot in addition to, or instead of, pain in the back or thigh. The first stage is usually regarded by the patient as an attack of lumbago and may vary in severity from a slight aching to a pain of such severity as to result in complete fixation of the spine by muscle spasm, rendering the patient incapable of any movement. This pain often radiates to the buttock and the back of the thigh on one side, but seldom extends below the knee. Examination at this time may show some limitation of spinal movement; flexion and extension being more limited than lateral movement, and the pain may be aggravated by the elevation of the extended lower limbs. It is unusual to find any local tenderness in the back unless muscle spasm is severe and no motor, reflex or sensory disturbance is to be found in the lower limbs. As a rule this initial pain subsides slowly after a period of rest, which may be a few days or several weeks. Recurrence is common, however, and may follow a further quite trivial injury or strain. The pain in this phase is a result of damage to the posterior common ligament and possibly to neighbouring ligamentous structures, and the stage has thus been set, by weakening of the retaining ligaments, for a disc protrusion to take place, but it is probable

that the actual protrusion does not occur at this time. Inman and Saunders (1942) observed that pain arising in damaged ligaments may be referred to the region of other deep structures having the same innervation, and on this basis it is possible to explain the early radiation of pain to the buttock and thigh, the pain itself being due to local spasm in the hamstring and gluteal muscles.

Pain in the leg and foot may follow the initial symptoms after an interval which varies from a few weeks to months or even years. The onset is sudden and is often associated with recrudescence of the original pain in the back. The two pains differ qualitatively in that the leg pain has a superficial burning character unlike the deep aching in the back; it is often aggravated by coughing and has, in fact, all the features of root pain.

Less common symptoms which may be encountered are weakness or paralysis of muscles acting on the affected foot, impairment of sphincter control, and intermittent cramps in the leg which may resemble intermittent claudication (O'Connell, 1943; Wolman, 1949).

The *physical signs* are now likely to be more extensive. Spinal movement is impaired and there may be a deformity having the appearance of a scoliosis, but in fact due to elevation of the pelvis on the affected side with flexion of the hip. The normal lumbar lordosis is flattened and may be replaced by a mild lumbar kyphosis. Lasègue's sign (limitation of straight-leg raising) is invariably present, and indicates increased tension upon a nerve root together with some degree of spasm of the paraspinal muscles. Minor degrees of muscle weakness may be found, particularly in the long flexor or extensor of the great toe. The ankle reflex may be depressed or absent. Impairment of perception of pin-prick over the dorsum of the foot is commonly found and may represent the area of distribution of part of the fifth lumbar or first sacral nerve root according to the finding of hypoæsthesia on the medial or lateral aspect of the foot respectively. Flabbiness of the calf muscles is pronounced and may be accompanied by a minor degree of muscle wasting. It is probable that these latter phenomena are reflex in origin, since neither condition would be likely to follow interference with a single nerve root.

To summarize, the characteristic history associated with prolapsed intervertebral disc is one of initial trauma followed by pain in the back, which in turn is followed by root pain in the distribution of one or more of the component roots of the sciatic nerve. The associated physical signs indicate, for the one part, local injury to ligamentous structures in the back, and for the other part, interference with the fifth lumbar or first sacral nerve root.

SCIATICA DUE TO INFLAMMATION OF MUSCULAR AND FASCIAL STRUCTURES

The diagnosis of this condition may present considerable difficulty, and often rests upon the absence of a characteristic history and signs of prolapsed intervertebral disc. It has already been mentioned that injury to

ligamentous structures in the lumbar spine may result in reference of pain to those deep structures of the buttock and thigh having the same innervation, and this concept is equally applicable to inflammation of the same structures.

The nature of "fibrositis", both in the lumbar region and elsewhere, is still to some extent obscure, but Copeman and Ackerman (1947) and Copeman (1949) suggested that lumbar fibrositis is due to fat herniation through the superficial fascia. These herniations may be felt beneath the skin, and pressure thereon reproduces the patient's pain. Relief of pain follows the excision of the nodule or local injection of procaine.

There are certain predisposing factors toward this condition: exposure to dampness or cold, unaccustomed physical effort, faulty posture, and a general tendency to attacks of "fibrositis". The onset of pain is usually sudden, but unlike that of disc lesions it tends to increase in severity over a period of hours or days. The pain is most commonly felt in the midline in the lumbar region, but may radiate to one or both buttocks and the backs of the thighs. It is aggravated by movement and relieved by recumbency.

The *physical signs* vary: local tenderness is constant, and tender nodules may be found in the paraspinal muscles or along the iliac crests. Some degree of spasm of the erector spinæ is often present without any spinal deformity and with a relatively free range of spinal movement. Lasègue's sign may be positive but the pain so elicited is referred to the back of the thigh and buttock, unlike the pain of disc protrusions which is referred to the back. No disturbance of motor, reflex or sensory functions can be demonstrated in this type of sciatica.

Diagnosis.—Confirmation of the diagnosis may be obtained by applying *the procaine injection test* introduced by Steindler and Luck in 1938. These authors put forward five criteria for a diagnosis of fibrositic pain:—(1) Contact with the needle aggravates the local pain; (2) contact with the needle elicits referred pain; (3) procaine suppresses local tenderness; (4) procaine suppresses referred pain; and (5) freedom of leg and spine movement is restored.

The performance of this test may in some cases bring about permanent relief of symptoms in addition to confirmation of the diagnosis.

SYMPTOMATIC SCIATICA

Pain in the course or distribution of the sciatic nerve may result from the presence of any condition which interferes mechanically with the nerve or its roots. Any intrapelvic mass may impinge upon the sacral plexus and thus cause pain referred to its branches. It is natural that this form of sciatica should be more common in women with their greater liability to various forms of pelvic tumour. Pain of this kind is common in pregnancy and is generally thought to be due to pressure by the fœtal head; as would be expected such pain is relieved by lying down and aggravated by standing or walking. Intervertebral disc prolapse, however, occurs during pregnancy,

and Capener (1944) has suggested that the concomitant flattening of the lumbar spine and the forward strain imposed by the gravid uterus predispose to this condition.

Carcinoma of the rectum, prostate gland or uterus may present with sciatic pain, and the importance of routine pelvic examination cannot be too strongly emphasized. Pain in the buttock and thigh may result from almost any pathological condition of the hip joint, since this structure receives the greater part of its extensive innervation through the sacral plexus. Local tenderness and limitation of hip movement usually provide the key to the diagnosis.

Tumours of the cauda equina may in their early stages produce symptoms and signs suggestive of disc prolapse. The signs, however, are likely to be extensive and bilateral, and when doubt exists the diagnosis can usually be established by X-ray and lumbar puncture.

Finally, the early pain of herpes zoster may occur in the course of the sciatic nerve, and it may be some days before the characteristic eruption makes the diagnosis obvious.

ACCESSORY METHODS IN DIAGNOSIS

X-ray examination of the lumbar spine, hips or pelvis may reveal gross bony abnormality to account for sciatic pain, but without the use of contrast media it is of relatively little value in the diagnosis of prolapsed intervertebral disc. Comparison of the relative sizes of the intervertebral spaces is unreliable, and no marked difference in these spaces could logically be expected, for it is only a small part of the disc that is extruded. It is also important to bear in mind that abnormality of the fifth lumbar vertebra is very common; Brailsford (1928) found developmental abnormalities in this region in 26 per cent. of 3000 X-rays of the lumbo-sacral region. The intrathecal injection of iodized oil or of air before X-ray examination may reveal the presence of a disc prolapse, but the method is not entirely reliable, since both false positive and false negative results may occur; the procedure is also not without danger. It is considered that a correct diagnosis can be made clinically in the majority of cases, and that contrast radiography should be reserved for those occasions when much doubt exists or there is possibility of a spinal tumour.

The value of *lumbar puncture* is small; Mixter and Barr (1934), Love (1938-39), and Walsh (1939) considered a rise in protein content of the cerebrospinal fluid to be usual with disc prolapse; later observers (Pennybacker, 1942; O'Connell, 1943; Kendall, 1947) found a normal protein content in the majority of patients. Subarachnoid block is rare, and can only occur when a disc protrusion is of such a size as to fill the lumbar canal.

TREATMENT

Gowers and Taylor (1899) stated that sciatica, although subject to recurrence, was a self-limiting disease, the prospect of ultimate cure being

good. Since there is no reason to presuppose any major change in etiological factors it must be assumed that the opinion of these two authorities still holds good, and enthusiasm for drastic surgical procedures should be tempered by the prospect that ultimate cure is likely to occur spontaneously or as a result of conservative treatment.

In general, there are two methods of treatment of the patient with *prolapsed disc:* conservative, by rest with measures to alleviate pain in the early stages; or surgical, by removal of the protrusion. The former method should in all cases be given an adequate trial. Rest must be complete in the sense that no weight-bearing by the spine should be allowed. The patient must be confined absolutely to bed although freedom of movement in bed is permitted. Complete immobilization with or without a plaster bed does not materially shorten the duration of symptoms, and has the disadvantage that stiffness of the legs and spine with painful flat feet are common sequelæ. Relief of pain in the early stages is usually obtained by the administration of mild analgesics and the application of heat to the lumbar region and legs. As soon as symptoms begin to subside, graduated bed exercises should be started, but these should be discontinued if they cause pain. The patient should not be allowed to leave his bed until there has been freedom from pain for several days, and any recurrence of pain after getting up is an indication for further rest. At this stage it is common to find that the physical signs persist in the absence of symptoms, and their presence may continue for many months after all pain has ceased.

Immediately upon resuming activity the patient should be fitted with a corset to support and prevent excessive movement of the lumbar spine. Plaster jackets are cumbersome and inefficient and do not appear to have any advantage over a well-fitted corset. A warning must be given against any violent exertion or heavy lifting for a period of at least six months, and the corset should be worn for a year. In this way the majority of patients obtain lasting relief from their symptoms. Spinal manipulation has no part to play in the treatment of disc prolapse; when once the diagnosis is established this procedure may, in fact, be highly dangerous, with the risk of converting a simple sciatica into a paraplegia. Attempts to dispense with the initial period of rest by application of a plaster jacket to the dorsal and lumbar spine are usually unsuccessful, since the resulting partial immobilization of the lumbar spine does not relieve the affected region of weight-bearing.

Before deciding that operation is necessary certain criteria must be fulfilled. The history must be a long one, usually consisting of several distinct attacks. Conservative treatment must have had an adequate trial and have failed to give relief. The patient's occupation must be considered; should this be heavy, with liability to repeated trauma to the back, operation may be essential to ensure freedom from recurrence. Finally, due consideration must be given to the patient's willingness to undergo a major surgical procedure.

The results of surgery are generally very satisfactory. Relief of pain is immediate and return to activity is rapid. Most patients are ambulant within three weeks of operation and are able to resume even the heavier occupations within three to four months. The wearing of a supporting corset is again advisable for a year following operation.

The treatment of *myofascial sciatica* is usually simple and satisfactory. Symptoms respond rapidly to rest and the local application of heat, with the possible addition of massage and exercises. If definite tender nodules are found these should be injected with a 2 per cent. solution of procaine, repeated on more than one occasion, if necessary. A search should be made for chronic sepsis, although it is doubtful whether this plays an important part in symptom production; it is, however, wise to treat any gross infection in the mouth or elsewhere.

Treatment of *symptomatic sciatica* requires no comment: removal of the underlying cause should be the aim. Intractable pain from inoperable pelvic tumours may require division of posterior roots, or spinal cordotomy.

CONCLUSION

Sciatica in its wider sense is a common symptom of a number of different pathological processes, the two most common being intervertebral disc protrusion and "fibrositis". The former condition produces a characteristic train of symptoms and signs and is as a rule responsive to conservative measures of treatment. Resort to surgery may be necessary in order to shorten the duration of a process which, although by nature self-limiting, may at times be tediously protracted.

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DISORDERS OF SLEEP

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Disorders of sleep constitute a large share of the problems with which the general practitioner has to deal, and the worry that they cause him is proportionately greater than that of any other single complaint. Insomnia alone is so common and causes so much distress to the sufferer that it leads to frequent and repeated requests for advice. The physician who has to give that advice soon learns to realize that individual sleep requirements vary greatly, that the personal response to sleeplessness is widely different, and that the underlying cause, often a neurosis, influences the picture of that response. He learns, too, that knowledge of the wide range of sleep requirements and sleep behaviour is essential to the reasonable management of disorders of sleep in individual cases.

NORMAL SLEEP

Normal sleep requirements change with age, and since the sleep pattern in childhood is so different from that in adult life, and since its disorder is really a separate problem, this short discussion will be limited to disorders in the adult. Most people require eight hours of sleep, or more, and the number who boast that they do not require more than five or six hours is small indeed. On the other hand, most of those people who have to manage with less than seven hours of good sleep, for any reason at all, would benefit by more. It must be remembered, too, that the amount of sleep needed for an individual's well-being is determined by what he feels he needs, and not by what other people, including the doctor, think is reasonable. If he feels he needs ten hours and in fact he can only get eight he will in the end suffer. The amount of sleep varies with the intensity of intellectual occupation, and it is a sad fact that those whose daily work is most intense and prolonged, such as medical practitioners, have the least opportunity for adequate sleep.

Apart from the duration of normal sleep, its pattern must be understood. When the depth of sleep is studied in a large number of normal adults it is found that different types of sleep behaviour exist. The most common is to find that two periods of very deep sleep are separated by a period of relative lightness in the early hours of the morning. The subject goes to sleep and quickly enters a period of deep sleep from which he can only be aroused with difficulty. From this time onwards his sleep slowly becomes lighter until 3 or 4 a.m., when he may become restless and disturbed, or actually wake momentarily. Sleep then deepens until about 6 a.m., and after an interval it rapidly becomes lighter and lighter until the normal person

wakes at his normal time, refreshed and satisfied. Some normal people only show one of these troughs of sleep, one group will slowly awaken from the early hours onwards, another will sleep most deeply as the night advances. There are clearly wide differences in the pattern of normals in this respect, but disturbances of sleep must be considered against this background. The amount of motor activity and dreaming also varies within wide limits of normal. Lastly, once the normal person is awake he does not desire sleep throughout the day until late evening is reached.

Disorders of sleep may be divided as follows for the purpose of this discussion:—

(1) Disturbances in the amount of sleep
  (a) Too little—insomnia.
  (b) Too much—somnolence or hypersomnia.
(2) Disorders of sleep incidence
  Narcolepsy and reversal of rhythm.
(3) Disturbances related to sleep
  Sleep paralysis, hypnagogic hallucinations, cataplexy, somnambulism, enuresis, night terrors, and nightmares.
(4) Disturbances occurring in sleep
  Epilepsy and migraine.

Some of these disorders are uncommon and some unimportant in the present context.

INSOMNIA

There are three main kinds of insomnia:—

(1) Delay in falling to sleep, called *initial insomnia* or *predormital insomnia*. This is by far the most common, and it is associated with the capacity to sleep deep and late as the night progresses. It is seen particularly in times of anxiety and tension. In this form of insomnia the first trough of deep sleep described in normal subjects is lost, the second retained or exaggerated.

(2) Intermittent restless sleep throughout the night. This is often associated with disturbing dreams, and is particularly likely to occur with advancing age in the absence of evident psychological stress.

(3) Awaking too early—*terminal insomnia*. In this form the subject loses the second trough of deep sleep, so that his sleep gradually becomes lighter until he awakens in the small hours, unable to go to sleep again. Going to bed later does not usually affect this form of insomnia, for the sufferer appears to acquire the habit of awakening at an earlier hour. He may have to accept the necessity of going to bed earlier than he would wish so that he can get seven hours sleep from 9 p.m. to 4 a.m., having made the maximum use of his ability to fall asleep and to sleep deeply as soon as he retires. This is particularly the case in elderly people, who require one or two hours less sleep than other adults, and who in consequence do not suffer any ill-

effect from awakening early, except the frustration and boredom of lying inactive in bed.

EFFECTS OF INSOMNIA

A great deal of experimental work has been undertaken into the effects of prolonged sleeplessness, and physical changes have been described in such circumstances. In particular, Kleitman (1939) studied bodily function after periods of continued wakefulness lasting for several days. In these experiments, however, animals and men were kept awake for prolonged periods and the condition did not simulate that of the insomnias which have been listed. However badly a patient sleeps, and more especially however badly he *thinks* he sleeps, several hours of good sleep are usually obtained each night, less than five hours sleep being exceptional. The story that "I don't sleep a wink" is usually honest but is rarely true. In the circumstances in which insomnia is met in general practice therefore physical accompaniments may occur, although they are not the result of the insomnia alone. When there are signs of physical deterioration it would be wise to ascribe them to the *cause* of the insomnia, whether that be physical or psychological, and not to the insomnia itself. On the other hand, grave psychological effects may follow prolonged sleeplessness. The distress which goes on to tension and anxiety, and the depression which may even lead to suicidal ideas need not be brought to notice. It is nevertheless important to realize that when this train of psychiatric deterioration results from insomnia, the insomnia itself is usually due to a psychological disturbance. There is all the difference between a normal subject lying awake, comfortable and placid, if a trifle discontented, and an anxious patient lying in bed, tense, restless and emotional. In both instances the insomnia may be the result of preoccupation, but in the first there is normal anxiety, whilst in the second the anxiety is abnormal and carries with it all the related disturbance of affect. Furthermore, the tense anxious patient who cannot sleep has not only to carry the added load of the distress of his insomnia; he worries about that in its turn and he also loses the beneficial relaxation which prolonged deep sleep will give him. It follows that insomnia must not only be considered against average sleep requirements and the individual's usual needs, but against the physical and mental basis upon which the insomnia has arisen. However seriously the physician may regard the problem of insomnia, and whatever care he may take, he is unlikely to help his patient to the best of his ability if he fails to study the causes of the lack of sleep *in each individual.*

CAUSES OF INSOMNIA

In any one patient there may be several contributory causes for loss of sleep, but they can be divided into three main groups: (1) constitutional; (2) physical; (3) psychological.

The *constitutional* variations in the amount of sleep a subject needs have

been mentioned. They vary with age, occupation, past sleep habits, and personal idiosyncrasy. Their recognition is mainly important in assessing the significance of the claim of lack of sleep in any one case.

The *physical* causes include those in the patient's environment as well as those due to his bodily state. Such factors as noise, light, cold, and discomfort must be considered. Here it is interesting to recognize how selective everyone is in response to changes in his environment in sleep. The town dweller cannot sleep in the silence of the country, but although he will sleep through the din of traffic, the clang of a nearby bell, or the whistle and roar of a passing train, he will awaken instantly at an unusual little noise in the house. On the other hand, he may not awaken with a start, as his wife will, in response to an insignificant human noise in the nursery.

The most obvious physical cause of loss of sleep is pain of any sort, but there are many physical disorders that are associated with insomnia for no apparent reason: endogenous toxic states, including most infections, and exogenous toxins, particularly beverages containing caffeine; alimentary disorders, which include the interesting occasional indiscretion of diet which we all know, will cause insomnia without any actual physical discomfort; arteriosclerosis and hypertension; organic brain disorder; and endocrine disturbances such as thyrotoxicosis. These are just a few of the physical illnesses which will cause a disturbance in the normal rhythm of sleep without any apparent physical symptoms being responsible. The most dramatic example of this state of affairs is the inversion of the sleep ratio after encephalitis lethargica: a physical disturbance in the brain leads to a profound change in the sleep rhythm in the absence of other physical or psychological causes for the sleep disturbance.

Psychological causes are by far the most common in insomnia. So much is this the case that in the absence of pain or evident physical causes inquiry will usually reveal a mental disturbance. This may range from fatigue or reasonable worry, include anxiety states or obsessive compulsive states, and extend to the psychoses. It must not be assumed, however, that because a psychological cause is responsible for the insomnia it is necessarily evidence of psychiatric abnormality in the patient. Prolonged overwork, great anxiety or responsibility, and excessive stress of any kind will in a stable person cause insomnia without other evidence of a neurosis. In these the outlook is good. When a neurosis is present the prognosis is that of the neurosis. Of the neuroses, those associated with tension (anxiety states, obsessive compulsive states, and fatigue states) are more likely to be associated with sleeplessness than are those in which depression predominates. The depressive often sleeps well.

MANAGEMENT OF INSOMNIA

What has already been read makes it clear that there must first be a detailed history and examination, each individual's insomnia being considered against

general experiences, the patient's needs, and his physical and mental state.

The main causes must then be dealt with, whether these are in the environment of the bedroom, in the patient's physical health or in his emotional state. As consideration of these factors includes a great deal of the routine work of general practice, they are beyond the scope of this discussion. There are a number of excellent articles and books, notably those by Nathaniel Kleitman (1939), T. A. Ross (1932), R. D. Gillespie (1929), H. Crichton-Miller (1930), and Meyer Solomon (1945), which are listed at the end of this article, and deal in detail with the social and psychiatric management of insomnia. In leaving this important aspect of management inadequately treated, it might be stated that most practitioners to-day labour under such pressure of work that they also are forced to leave it in the same unsatisfactory state.

MEDICAL TREATMENT OF INSOMNIA

Reviews of the pharmacological treatment of insomnia have been written for *The Practitioner* by Feiling (1932), Watson Smith (1945), and Chambers and Alstead (1948). Other excellent reviews are by Soma Weiss (1936) and by Goodman and Gilman (1941).

There is no question that the use of hypnotics has in most cases a valuable place in the treatment of insomnia. There is no need for a patient to suffer from persistent and serious lack of sleep for the lack of one of the harmless sedatives which are available to-day. It is true that far too many barbiturates are given indiscriminately to patients, and that the public swallows them avidly, without due thought, but this fact does not detract from their value when administered with understanding and care. Solomon (1945) deals with this debatable point in some detail, and in arguing for their use says: "As a matter of truth, if hypnotics are not used for insomnia, one can never be sure that other measures will produce sleep". Ross (1923), in discussing insomnia in the common neuroses, pointed out that we can be as unscientific in withholding hypnotics as in giving them injudiciously. Having argued in favour of the use of hypnotics, Solomon lists the precautions with which they should be used. In general it is clear that to give sedatives without attending to the basis of the insomnia is undesirable. When the decision to give them has been made, they should be given in adequate doses, in a form suitable to the kind of insomnia, they should be under the sole and continuous supervision of the practitioner, and the patient should be allowed no latitude or initiative in their administration. Only enough for a few days should be prescribed at a time and it should be made clear from the onset that their administration is temporary. The patient should be seen personally from time to time while he is receiving hypnotics.

The choice of drugs in the treatment of insomnia is enormous, and in particular the number of new barbiturates, many of which are very similar but have different trade names, leads to sheer confusion of choice. It would be wise therefore if each practitioner would choose a small number

of sedatives which he finds valuable and, having selected them, get to know their actions and side-effects, for to know a few well is better than to use many with less knowledge. Details of administration can be found in the earlier articles in *The Practitioner*, by Feiling, Watson Smith, and Chambers and Alstead.

Useful sedatives of choice are:—

(1) *The bromides* are mild sedatives which have the disadvantage that they do not give a satisfactory result for several days, as their action is cumulative and their excretion slow. Prolonged administration may therefore cause bromism, and acne is common. A dose of 10 to 30 grains (0.65 to 2 g.) of sodium bromide at night used to be usual, but now the bromides are largely replaced by the barbiturates.

(2) *Chloral hydrate* is much more rapid in action, gives a good sound sleep for six to eight hours, and usually has no unpleasant side-effects. Occasionally it may cause nausea and vertigo. Chloral appears to be safer than some books suggest, and given as chloral hydrate in 10-grain (0.65 g.) doses with the same amount of sodium bromide it is very useful in cases of acute secondary insomnia.

(3) *The barbiturates.*—The most widely used and presumably therefore the most satisfactory are:—

Phenobarbitone (luminal, gardenal), ½ to 2 grains (0.032 to 0.13 g.). An excellent mild hypnotic in moderate cases of insomnia, especially of the intermittent kind.

Barbitone (veronal) and *sodium barbitone* (medinal), 5 to 10 grains (0.32 to 0.65 g.), are absorbed quickly and excreted slowly, and so have a long action. They also tend to have a cumulative effect.

Butobarbitone (soneryl) leaves no "hangover" and secures up to six hours of good sound sleep in mild insomnia. The dose is 1 to 3 grains (0.065 to 0.2 g.). It is useful in initial insomnia.

Sodium pentobarbitone (nembutal), 1½ to 3 grains (0.1 to 0.2 g.), is rapidly acting and safe. It leaves no after-effects, and is of great value for the terminal form of insomnia, if taken on waking.

Sodium amytal, 1½ to 3 grains (0.1 to 0.2 g.), has a more marked and a more prolonged effect than nembutal, and is a safe barbiturate. It has the disadvantage that people vary in their response to it, and some complain of a slight "hangover". It is especially useful in the first two types of insomnia, but should be avoided in terminal insomnia; if used in terminal insomnia it should be taken at bedtime.

Sodium allyl barbiturate (seconal), 1½ to 3 grains (0.1 to 0.2 g.), is one of the short-acting barbiturates with no after-effects, which is well tolerated by most patients. It is useful in mild secondary insomnia.

Diallyl barbiturate acid (dial), 1½ to 3 grains (0.1 to 0.2 g.), acts rapidly and is of medium length in its duration. It is safe.

The analgesics and stronger hypnotics will not be discussed here.

Having briefly discussed the disorders resulting in lack of sleep, those causing excessive sleep will be mentioned. This is not the place to discuss them in detail for they are, in contrast to the insomnias, so very uncommon.

HYPERSOMNIA

Somnolence may occur through fatigue, or as a symptom of a psychological disturbance, usually of an hysterical kind, but somnolence of sufficient

degree to call for medical advice suggests the possibility of organic disease of the nervous system. When this is the case the lesion is usually in the region of the third ventricle, either in the basal grey matter or the upper brain stem. In consequence, pathological somnolence is usually associated with other evidences of organic disorder of the nervous system, including signs of high intracranial pressure. Other forms of somnolence to be borne in mind are those associated with pituitary disease (adiposo-genital dystrophy), and with toxic states, both endogenous, e.g. diabetes mellitus and uræmia, and exogenous.

NARCOLEPSY

This condition is easily recognized, for it consists of attacks of compulsive sleep. The patient *must* go to sleep, and having done so awakes refreshed, often after only a few minutes. This disturbance occurs repeatedly throughout the day: in buses, standing in queues, in conversation, or during a meal. To relax for a moment will in some cases inevitably result in an attack of sleep, particularly as the day advances. The suddenness and brevity of the attacks, as well as their stereotyped nature, makes the condition unmistakable. In addition it is often associated with attacks of *cataplexy* in which the subject suddenly feels weak and may fall down in response to sudden emotion, whether of amusement, anger, or fright. There is no loss of consciousness in cataplexy.

Narcolepsy is associated with organic disease of the neighbourhood of the third ventricle, including encephalitis lethargica, tumours, and injury, but if this is the case other evidence of the lesion is usually apparent. It also arises in association with pituitary disorder. More often it arises with no evident cause, in an "idiopathic" form. When it does so it usually persists throughout life. In the past, stimulants including caffeine were used, but amphetamine and its derivatives have proved of enormous value. The two most effective are benzedrine sulphate (5 to 10 mg.) and dextroamphetamine (dexedrine) (5 to 10 mg.). In narcolepsy large doses may be needed, and I have one patient with pituitary disorder whose narcolepsy is well controlled with dexedrine, 15 mg. three times a day. This is an exceptional dose, but it was reached by slow increase until a reasonable degree of wakefulness was attained. The patient will probably have to continue treatment indefinitely.

DISTURBANCES RELATED TO SLEEP

Sleep paralysis occurs as the patient is going to sleep or on waking. It consists of an inability to move the body voluntarily, although respiration, visceral activity, and reflex responses are normal. It may rarely be accompanied by a change in body sensation, or of the affective state. The patient is conscious, and on the first occasion very alarmed, but he learns to overcome the paralysis by an enormous effort of will. Although the condition is rare it is important not to assume that it is hysterical. It is often associated with narcolepsy and cataplexy. Its pathology is not known; attempts to explain

it have been philosophical rather than scientific, and there is no treatment.

Hypnogogic hallucinations are usually visual but may be auditory. They are vivid and sometimes alarming. Children are particularly likely to experience them, but they disappear as adolescence approaches. There is little evidence that they are psychogenic, but it is probable, as they occur in the period of going to sleep or awaking, that they are related to sleep paralysis and that they are, as Gowers said, due to "an insubordinate action of the lower centres, occurring during the gradual withdrawal of the higher control". Abnormal states of bodily sensation or of affect, and myoclonic jerks occur in the same period of going to sleep or waking, and the main importance in their recognition is to realize that they occur in otherwise normal people and do not require any treatment beyond reassurance.

Somnambulism, enuresis, night terrors, and nightmares may well be considered together for the purpose of this discussion, because they all occur, alone or together, in similar circumstances. They are all most common in childhood, particularly between the years of five and fifteen, and they are often associated with other evidence of an infantile neurosis. Sometimes somnambulism or enuresis is a manifestation of epilepsy, and this must certainly be borne in mind. Sometimes, too, enuresis is the result of physical disease and nightmares are associated with toxic states, but in the great majority of instances these disturbances of sleep are related to emotional tension. In the child, this is a reflection of instability in the child himself, or of insecurity in his home background; in the young adult it may be evidence of an anxiety state or an early psychosis. Management in most cases is therefore mainly psychiatric, aimed at an understanding of the cause of the neurosis, its sympathetic management, and an explanation of the mechanism of the symptoms. Any other approach, particularly in the case of enuresis, will probably do more harm than good: any reproof, and indeed any attention to the condition, may well perpetuate it. Once more the detailed management of these conditions must be left to fuller works, particularly those by Gillespie (1929), and Ross (1923, 1940), for it is apparent that to do more than to present the disorders of sleep in a systematic manner would be beyond the capacity of this article.

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VITAMIN DEFICIENCY AND THE NERVOUS SYSTEM

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In this country the neurologist is rarely able to attribute disease of the nervous system to vitamin deficiency. Although in the majority of his cases the cause of the nervous disturbance is not known, indications of vitamin deficiency remain very meagre. Yet he knows that the nervous system *can* be disordered in such a way and that striking neurological syndromes have been described. Indeed, he recalls that it was the study of a neurological affection—beriberi polyneuritis—which led to the discovery of vitamin B and gave such an impetus to the search for essential food substances. He knows, too, that apart from pellagra, from time to time clinicians working in warm climates, in different parts of the world, have recorded certain peculiar neurological symptoms and signs in malnourished natives. More recently, during the late war, further evidence came his way which pointed to defective nutrition as one important cause of serious disorder within the nervous system. Finally, there is evidence from the experimental laboratory: several members of the vitamin B complex—thiamine, riboflavine, pyridoxine and pantothenic acid—appear to be essential for the normal function of the nervous system in certain species. To the neurologist, then, the further pursuit of the vitamins is of considerable interest.

EXPERIMENTAL EVIDENCE

Animal experiment has shown that deficiency of vitamin A, vitamin E, and of various components of the B complex may lead to neurological disorder. But only the vitamin B complex is known to be of importance to the *human* nervous system.

Vitamin A.—In growing animals deficiency of vitamin A may produce degeneration in the brain, the spinal cord, and certain cranial and spinal nerves. One factor in the production of the lesions is the mechanical compression and deformation of the affected structures as a result of the inadequate development of the skull and vertebral column. The skeletal and nervous systems do not develop in harmony, so that cranial and spinal cavities and foramina are undersized and overcrowded. But apart from this mechanism there are also indications that vitamin A deficiency leads to unequal disturbance of growth of the various tracts of the spinal cord. The significance of these observations in relation to nervous disease in man is not known.

Vitamin E.—Pathological changes in the spinal cord and muscles develop

in some young animals when suckled by mothers deficient of vitamin E. In newly hatched chicks, degeneration in certain areas of the cerebellum and brain stem has also been described in vitamin E deficiency. So far, however, the value of vitamin E in neurological disorders has not been demonstrated. Certainly, in the muscular dystrophies and in motor neurone disease vitamin E is not beneficial.

The vitamin B complex.—It appears that several members of the vitamin B complex are essential for nervous activity. The chief function of vitamin B_1 (thiamine) is related to one of the most elementary of life processes—cell respiration. It plays a significant part in carbohydrate metabolism, and when it is missing a disturbance arises in the pyruvate enzyme system. Deficiencies of riboflavine, nicotinic acid, pyridoxine, pantothenic acid, in different experiments, have all been shown to produce neural degeneration and abnormalities.

In the majority of nervous disorders in man a primary dietary deficiency of these vitamins can be excluded. But this does not mean that there can therefore be no derangement of the normal rôle of these substances as they affect the nervous system. We know that a vitamin can be inactivated by an exogenous or endogenous toxin, and that susceptibility to experimental infection of the nervous system can be shown to be dependent upon vitamin deficiency. Then, also, there is the question of the synthesis of these vitamins in the human intestine and the possibility that functional disturbance in the intestinal tract may lead to neurological disorder.

A chemical test for the presence of vitamin in the human body may give a satisfactory result when a biological test might indicate that the natural rôle of the vitamin has ceased. The notion of anti-vitamins and toxamins in respect of nervous disease is new and unexplored. Lastly, there always remains the possibility that antenatal deficiency, however produced, might lead to lesions of the nervous system which become manifest after birth. There is little to support the old view of "abiotrophy" as an important explanation for degeneration of the nervous system.

CLINICAL EVIDENCE

(1) *In Temperate Climates*

Polyneuritis, subacute combined degeneration of the spinal cord, and Wernicke's encephalopathy are three neurological disorders which occur in this country, and appear to arise from defective nutrition of the nervous system. But in none of them is it a matter of mere lack of some essential substance in the diet.

Polyneuritis.—There are three forms of polyneuritis in which nutritional factors seem to be of etiological importance—alcoholic polyneuritis, the polyneuritis of some gastro-intestinal disorders, and the polyneuritis of pregnancy. In such affections as diphtheritic polyneuritis, acute toxic

polyneuritis, and diabetic polyneuritis there is no evidence of vitamin deficiency, and no acceleration of the processes of recovery can be demonstrated following treatment with vitamin B_1. In alcoholism, polyneuritis does not develop while there is a satisfactory food intake, including the components of the vitamin B complex. When neuritis has developed there is always evidence of gastritis, anorexia, loss of weight, depressed liver function, and perhaps vomiting and diarrhœa. The results obtained by intensive treatment with vitamin B_1 and a nutritious diet, although not dramatic, generally support the view that the nerve lesions are nutritional in origin and are not directly due to alcoholic intoxication.

Occasionally, polyneuritis will develop in a patient suffering from some chronic gastro-intestinal disorder, such as dysentery, ulcerative colitis, pyloric or jejunal stenosis, or following operative procedures on the intestinal tract. Pellagra has been observed in such cases. Presumably the absorption of vitamins and their synthesis by the intestinal bacteria are deficient. Elderly patients with poor appetites seem to be more prone to such complications.

Polyneuritis in pregnancy is an uncommon event and the evidence of nutritional disturbance is not very convincing. It is known that nutritional requirements are increased in pregnancy, and certainly in countries where beriberi and pellagra are endemic the pregnant woman is very liable to these diseases. In some cases hyperemesis precedes the onset of the paralysis. Retrobulbar neuritis may be present. The effects of treatment with vitamin B complex are not convincing.

Subacute combined degeneration of the spinal cord.—In this disorder we have an example of serious degeneration of the spinal cord which is associated with a known disturbance of gastric secretion. It cannot be said that the disease is a nutritional disorder, in the sense that it is due to dietary deficiency, but its close association with pernicious anæmia indicates that a similar deficiency of some essential substance is responsible for the changes in the nervous system. Folic acid, a member of the vitamin B complex, can restore the blood picture to normal but has no effect on the cord changes and may, in fact, induce their development. Vitamin B_{12}, on the other hand, seems to benefit both blood and spinal cord disorders and it is present in liver. Although there have been reports of "dramatic" improvement in patients suffering from cord degeneration following the use of vitamin B_{12}, the evidence is still slender, and much more work will have to be done before it is shown that it excels liver therapy. In my experience, subacute combined degeneration is nowadays more often seen with a normal blood picture and bone marrow; anæmia is uncommon. Liver extracts, in doses of 30 ml. per week, intramuscularly, do not always produce satisfactory improvement, and it is to be hoped that the early reports of the beneficial effects of vitamin B_{12} will be confirmed.

Wernicke's encephalopathy.—For many years this uncommon disorder was

thought to be due to some effect of alcohol on the midbrain and brain stem. Later, its observation in the terminal stages of a chronic illness—carcinoma, for example—and the occasional association with hyperemesis gravidarum, suggested that some nutritional or toxic factor must be responsible. The characteristic hæmorrhagic lesions in the brain stem have been noted in infantile cerebral beriberi and in thiamine-deficient rats and pigeons. In foxes bred for their fur in captivity similar brain-stem lesions were observed if their diet contained sufficient quantities of raw fish. Ataxia, convulsions and paralysis then ensued, but the disease could be prevented by the addition of thiamine to the diet. It appears that the vitamin is inactivated or destroyed by some substance in raw fish. In the recent war in the Far East, Wernicke's encephalopathy reached epidemic proportions in some camps and the value of thiamine in treatment was conclusively shown. Sporadic cases are encountered in this country from time to time, but in many the origin of the vitamin deficiency state is quite obscure. I have seen the characteristic symptoms and signs develop and respond to treatment with thiamine in circumstances which did not suggest a primary dietary deficiency. If an elderly debilitated person develops a state of confusion with signs of ataxia and ophthalmoplegia the use of thiamine parenterally is always advisable. There are probably many factors which can lead to the essential disturbance of the disease.

(2) *In Warm Climates*

The following affections of the nervous system may arise in malnourished communities living in warm climates:—

Beriberi	Laryngeal palsy
Pellagra	Wernicke's encephalopathy
Retrobulbar neuritis	Spastic paraplegia
Nerve deafness	Lathyrism
Spinal ataxia	

In two of these maladies—the spastic paraplegia of the prisoner-of-war and lathyrism—there is no good evidence that vitamin deficiency plays an etiological part. The former disease was a rare one in certain prisoner-of-war camps in the Far East, but was nevertheless found mainly in a camp where beriberi, pellagra and other nutritional disturbances were particularly rife.

Lathyrism is a similar disease, in which the rapid development of spastic paraplegia follows the ingestion of lathyrus. Its association with the ingestion of certain pulses has been noted since the time of Hippocrates. He wrote: "At Ainos these men and women who continually fed on pulse were attacked by a weakness in the legs which remained permanent". The term "lathyrism" should be confined to those cases of epidemic paraplegia in which such association has been observed. There may be other causes for an outbreak but no useful purpose is served by speaking of "lathyrism without lathyrus". In Spain, I have had the opportunity of seeing examples of the disease. It

develops in the young adult male of poor communities when a certain amount of lathyrus meal has been used to supplement a meagre flour ration after a poor harvest. Not all who eat the lathyrus meal develop the disease, but the evidence suggests that the greater the consumption of lathyrus the greater the liability to paraplegia. Overnight, or within a week or two, stiffness and weakness of the lower limbs develop, often with much cramp and dysæthesiæ. There is no cerebral disturbance, the arms are usually spared, and no sensory alterations can be detected. The patient remains in good general health and presents no signs of vitamin deficiency. The damage to the spinal cord is usually permanent and little improvement takes place after a few weeks or months. It differs from the spastic paraplegia of the prisoner-of-war, in that cerebral disturbances in the early phase of the illness are lacking, there are no signs of vitamin deficiency in the community, and there is always evidence of the use of lathyrus flour. The acute onset of the disease and the permanent injury to the pyramidal tracts suggest that the responsible lathyrus factor acts in some way upon an essential enzyme process in the nervous system.

Beriberi.—In the infantile, cardiac, cerebral and wet forms of beriberi the rapid response obtained by the administration of thiamine parenterally is strong evidence that vitamin B_1 deficiency is the essential etiological factor. There is a profound disorder of metabolism in all forms of acute beriberi. In the chronic dry form of the disease, polyneuritis is the main lesion. Whether it develops rapidly or slowly, recovery is always a tardy process, irrespective of treatment with vitamin B_1. If there is an essential biochemical lesion of the peripheral nervous system in beriberi polyneuritis it seems that morphological changes set in which make any rapid recovery impossible. Certainly, the limited usefulness of thiamine in beriberi polyneuritis does not justify its being designated as the "antineuritic vitamin".

Pellagra.—Disorder of the nervous system may precede, accompany or follow the cutaneous, oral and alimentary lesions of pellagra. Neurological symptoms may be mild or fatal, acute or chronic, insidious or fulminating. Brain and spinal cord are more liable to be affected than the peripheral nervous system. In pellagrous communities much chronic mental ill-health is found. Acute mental disturbances, with stupor, delirium, muscular tremors and rigidities are a not uncommon development and respond with some success to the parenteral administration of nicotinic acid and other members of the vitamin B_2 complex. In chronic pellagra, degeneration of the lateral and posterior columns of the spinal cord may develop, a condition not unlike that found in subacute combined degeneration. But its response to vitamin B concentrates and to liver therapy is usually limited.

Retrobulbar neuritis, nerve deafness and spinal ataxia.—The curious neurological syndromes that developed among malnourished prisoners-of-war in the Far East and Middle East during the recent war provide the latest clinical evidence that nutritional deficiency can play an important part in

producing diseases of the nervous system. Retrobulbar neuritis, nerve deafness, spinal ataxia, and laryngeal paralysis occurred in considerable numbers in camps where starvation and deficiency syndromes were common. Why some men escaped altogether and others developed one or more of these disorders remains a mystery. Deficiency was gross and widespread, yet the neurological lesions which resulted were selective and discrete. Treatment with various fractions of the vitamin B complex and with other vitamins, plus a balanced diet, yielded quite inconclusive results. The natural history of these disorders points to some initial metabolic disturbance which was rapidly followed by more or less irreversible morphological changes.

CONCLUSIONS

There is no doubt that nutritional disturbances can effect serious and permanent injury to the human nervous system, despite the striking lack of pathological information in this branch of neurology. Contrary to expectation the general health of the affected person may remain quite good. The ordinary signs of malnutrition may be absent. Within the nervous system itself there may be widely dispersed and dissimilar lesions—in certain cranial nerves, in the cerebral hemispheres, in the midbrain, brain stem, spinal cord and in the peripheral nerves. Their onset may be abrupt or insidious, and although a certain amount of overlapping is encountered, clinical experience suggests that several different processes are at work. The resulting syndromes are, on the whole, distinctive. Certainly, one would not suspect after examining individual cases of, say, Wernicke's encephalopathy, spastic paraplegia of the prisoner of war, spinal ataxia, retrobulbar neuritis or nerve deafness, that they belonged to a group of affections which had in common such a fundamental disturbance as that of nutritional deficiency. The richness and diversity of the symptomatology of these disorders should be borne in mind when the rôle of vitamin deficiency in the production of diseases of the nervous system is under consideration.

Future research is not likely to disclose that dietary deficiency is the simple explanation. The evidence, such as it is, suggests that there are certain essential factors which influence the metabolism of nervous tissue in a number of ways. It is conceivable that in certain circumstances, dietary or otherwise, the activities of such substances are inhibited or perverted, and that certain elements of the nervous system suffer as a consequence. Clues to the existence of such mechanisms must be looked for.

ULCERATION OF THE MOUTH IN CHILDREN

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Ulceration of the mouth, from a variety of causes, is common in childhood. Infections are the principal cause, particularly infection with the herpes simplex virus. The causes of ulceration may be classified as follows:—

(A) *Fissures of the lips*
- Simple fissures
- Rhagades
- Cheilosis

(B) *Ulceration of the lips*
- Herpes labialis
- Impetigo contagiosa
- Septic ulceration
- Traumatic ulceration
- Ulcerating hæmangioma

(C) *Ulceration of the mouth and tongue*

Infective:
- Acute herpetic gingivostomatitis
- Recurrent herpetic stomatitis
- Thrush
- Abscess ulceration
- Vincent's infection
- Pyorrhœa
- Chickenpox or smallpox
- Diphtheria
- Infectious mononucleosis
- Tuberculosis
- Syphilis

Nutritional:
- Scurvy
- Pink disease
- Cancrum oris

Traumatic:
- Palatal
- Dental
- Foreign bodies
- Corrosives
- Drugs

Various:
- Allergy
- Leukæmia
- Agranulocytosis

These forms of fissuring and ulceration will now be considered seriatim.

FISSURES OF THE LIPS

Simple fissures.—These are common in children, particularly in states of febrile and chronic illness and malnutrition. They are usually slight and

have a strong tendency to heal with improvement of the general condition. Being superficial they do not leave permanent scars. Treatment consists in the application of a bland preparation such as lanoline to prevent drying; an antiseptic cream, such as penicillin cream, is preferable in the more severe cases.

Rhagades.—This manifestation of congenital syphilis consists of deep fissures at the angles of the mouth which involve both skin and mucosa. Permanent scarring remains at the site of the fissures.

Cheilosis.—A thickened macerated appearance of the skin at the angles of the mouth with radiating fissures is the distinctive feature of this disease. Formerly regarded as a low-grade infection it is now known to be a deficiency disease, since administration of vitamin B_2 complex rapidly cures the condition.

ULCERATION OF THE LIPS

Herpes labialis.—Sometimes known as "cold sores" or "fever blisters" these lesions often occur on the muco-cutaneous parts of the lips in the common respiratory infections, and sometimes in other acute fevers. The bunches of small blisters rupture in a day or two producing shallow ulcers from which serum oozes and forms crusts on drying. The tendency of children to rub and pick the lesions often causes secondary infection.

A filtrable virus, known as the herpes simplex virus, is now known to be the cause of herpes labialis. The primary infection with this virus usually takes the form of acute herpetic stomatitis (see p. 151), and herpes labialis, which is usually recurrent and tends to appear in herpetic subjects under conditions which favour the virus, is the most common manifestation of the resultant life-long infection. If unmolested, the crusts of the cutaneous herpes lesions prevent secondary infection and no treatment is indicated, but since they are likely to be picked in childhood, these lesions, in common with the more exposed mucosal lesions, should always be treated with an antiseptic ointment. It may sometimes be necessary to prevent persistent picking by splinting the arms.

Impetigo contagiosa.—The vesicles, ulcers and crusts of this common disease often involve the muco-cutaneous part of the lips. The nature of the lesions is rendered apparent by the presence of similar lesions in the adjacent part of the face. Penicillin, preferably given systemically owing to the difficulty of retaining cream on the lips, soon cures the condition. Penicillin cream or ammoniated mercury paste, 1 per cent., should be applied to the associated skin lesions after careful removal of the crusts.

Septic ulceration.—Septic ulcers may arise on the lips from infected fissures, herpes simplex, trauma, or subcutaneous infection such as cellulitis. Whatever their origin they should all be treated by the systemic administration of penicillin, most conveniently given to children by a daily injection of aluminium stearate procaine penicillin, and the local application of an

antiseptic cream. Septic ulcers of the lips should be regarded seriously and promptly, and be carefully treated to minimize the possibility of permanent disfigurement.

Traumatic ulceration.—Trauma of the lips involving the extrabuccal part should be carefully repaired with fine sutures if such are indicated, as in the case of a partial split, if permanent disfigurement is to be avoided. The cosmetic result of injury to the inner part of the lips is less important.

Ulcerating hæmangioma.—Cavernous hæmangiomas involving the lips occasionally ulcerate; they are particularly liable to do so in this exposed situation. The infection and scarring which follow ulceration almost inevitably cause permanent malformation of the lip. Deep X-ray therapy is probably the most successful form of treatment in this distressing condition.

INFECTIVE ULCERATION OF THE MOUTH AND TONGUE

Acute herpetic gingivostomatitis.—This acute disease is essentially a childhood infection, although it may occasionally occur in adult life. It is the principal cause of ulceration of the mouth in childhood. The disease is rare before the eruption of the first teeth, but from the end of the first year the incidence rises rapidly to a peak during the third year, and drops to a low level after the sixth. It is most common in the autumn and winter months.

Fever often precedes the mouth symptoms and ranges from 101° to 103° or 104° F. There is severe malaise and the painful mouth lesions cause much irritability and misery, and almost complete anorexia. Only bland fluids in limited amounts are tolerated at the height of the illness. Soon after the beginning of the illness the buccal mucosa becomes inflamed and the gums congested and swollen. Small superficial vesicles appear on the edge of the tongue, on the lips, cheeks and palate. The vesicles soon ulcerate and become secondarily infected with mixed organisms such as streptococci, staphylococci and *Monilia albicans* (thrush). The sloughing ulcers and accumulation of debris in the mouth produce a very foul breath. The submaxillary lymph glands show considerable enlargement. The disease is self-limiting and the fever usually subsides within a week. Healing of the ulcers is usually complete within two weeks.

Treatment consists of good nursing appropriate to a fevered, highly irritable child. Sedatives and hypnotics should be used freely to promote rest. At the height of the illness nourishment should only be given in fluid form: sips of cold bland fluid, such as milk and sugar and very diluted fruit drinks with sugar, should be given frequently *ad lib.* Oral hygiene is important and should be managed very gently: swabbing with hydrogen peroxide, half- to full-strength, to loosen large sloughs is useful in severe cases. Older children may be induced to wash the mouth out often with an antiseptic mouth wash such as glycerin of thymol. Young children should have borax and glycerin applied to the mouth several times a day; or gentian violet, 1 per cent. in aqueous solution, twice daily. A sulphonamide should be

given, in emulsified form for ease of administration, to combat secondary invaders; also systemic penicillin in severe cases.

This form of acute stomatitis is now known to be the primary infection with the herpes simplex virus, as a result of which a latent infection with the virus is established and maintained throughout life. Following the primary infection the host remains entirely asymptomatic unless circumstances favourable to the virus arise, such as respiratory tract infection, when it is able to assert itself and cause an herpetic eruption. After the age of six years susceptibility to the primary infection is very low and the possibility of becoming an herpetic subject correspondingly remote. Although typically situated in the mouth, the primary infection may occasionally be located elsewhere, such as on the skin, eye or vulva. Recurrent or secondary herpes, which unlike the primary infection causes only a mild local reaction and little or no systemic disturbance, may be located not only on the lips, which is the most common site, but also on the face, eye, buccal mucosa, tongue, genitals, and occasionally elsewhere on the skin. Encephalitis is occasionally caused by the herpes simplex virus, also herpes zoster which, however, is characteristically caused by a specific zoster virus. The primary infection is followed by a persistently high antibody titre, indicating a degree of immunity which precludes further exogenous infection. The virus is readily transmitted to those who are susceptible, and herpetic lesions on the lips of adults are a common source of infection in children. The primary disease usually appears within ten days of exposure.

Recurrent herpetic stomatitis.—This is one of the recurrent forms of herpes which may occur in herpetic subjects. It sometimes accompanies herpes labialis. The local reaction is mild, although the exposed nerve endings in the ulcers may be rather painful, and there is no general illness. Soft, non-irritating food and bland fluids should be given to minimize local irritation.

Thrush.—This infection, caused by the fungus *Monilia albicans*, is common in young infants, particularly in institutions. It also occurs in debilitated older infants and in young children as a secondary invader in ulcerative conditions of the mouth. The lesions are whitish, adherent colonies on the buccal mucosa and tongue. The condition may subside without treatment, but it may spread over a considerable part of the oral mucosa giving rise to ulceration and secondary infection. Since there is always a risk of serious complications, such as œsophagitis which is often fatal, immediate isolation to minimize the risk of cross-infection, and bi-daily swabbing of the mouth with 1 per cent. gentian violet in aqueous solution, should be routine procedures.

Abscess ulceration.—The most common forms of abscess to rupture into the mouth are apical dental abscesses (gumboils) and supratonsillar abscesses (quinsy). Treatment should consist in the administration of penicillin, and in surgical incision, preferably before ulceration occurs.

Vincent's infection.—Vincent's organisms are saphrophytic and never cause a primary infection in a healthy mouth, but only secondary infection in individuals whose mouths have been damaged by other infections or traumatic lesions, or whose general resistance is poor. It often follows gingivitis, especially in those of poor economic status suffering from malnutrition and in whom oral hygiene is poor. There is general malaise, and fever may be present. The infected ulcers are covered with a grey necrotic membrane. Affected gums have a swollen, inflamed, necrotic appearance; they bleed readily and are very tender.

Treatment consists first and foremost in the correction of malnutrition. Local treatment comprises cleansing the mouth several times a day with swabs dipped in hydrogen peroxide. In older children frequent flushing of the mouth with a hydrogen peroxide or other antiseptic wash is preferable. In severe cases systemic penicillin helps to eradicate any pyogenic infection. Arsenical preparations, formerly so popular, are of doubtful value.

Pyorrhœa.—This is rare in childhood. It is a mixed infection which is usually secondary to deficiency states or drugs which cause gingivitis. It is a common complication of scorbutic gingivitis. The first principle of treatment is to find and treat the underlying cause. Correction of this, an optimal diet and the use of antiseptic mouth washes or sprays will soon cure the disease.

Chickenpox and smallpox.—In both of these exanthemas a few vesicles are usually to be found in the mouth. Their presence is of diagnostic value in cases of chickenpox with doubtful skin lesions.

Diphtheria.—Diphtheritic ulceration may involve the fauces and posterior part of the palate.

Infectious mononucleosis.—Ulceration may occasionally spread from the throat to the mouth in this disease. Sore throat is common in children who suffer from this disease.

Tuberculosis.—Chronic indolent ulceration of the mucosa of the lips or mouth, with non-tender enlargement of the associated lymph glands, should always suggest the possibility of a primary tuberculous lesion. Although uncommon, these lesions are not rare, and are usually missed.

Syphilis.—Syphilitic manifestations in the mouth in childhood are usually congenital. In young infants mucous patches and moist papules may occur and both may ulcerate. Other manifestations, such as snuffles, splenomegaly, and osteitis, should indicate their nature. In older children with congenital syphilis gummas may develop in the mucous membrane of the lips or mouth, or in the tongue. Ulceration of these lesions may occur; a perforation in the soft palate should always suggest the possibility of congenital syphilis.

NUTRITIONAL ULCERATION OF THE MOUTH AND TONGUE

Scurvy.—In infantile scurvy, most often seen between the ages of six and

eighteen months, purplish swelling of the gums is a common feature. It occurs only in the vicinity of erupted teeth, particularly around the incisors. In severe cases the gums are friable and bleed easily, and secondary infection with pyogenic and Vincent's organisms may cause considerable gingival ulceration. Large doses of ascorbic acid (vitamin C), 100 mg. t.d.s., relieve the pain in a day or two, and healing of the lesions is rapid. A well-balanced diet should prevent any recurrence.

Pink disease (*erythrœdema*).—This disease of unknown etiology, in which the principal manifestations are sweating, muscular hypotonia, anorexia, loss of weight, photophobia, insomnia, great irritability and swelling and redness of the hands and feet, is most often seen between the ages of six months and two years; large, shallow, indolent ulcers may appear in the mouth. These ulcers are most often seen in the front of the mouth, on the lips, cheeks or gums. Their nature is uncertain, but malnutrition caused by the prolonged disease is probably the chief cause, with infection a subsidiary factor. An adequate, well-balanced, bland diet must be given if possible, and liberal amounts of all the vitamin concentrates should be added, particularly the B complex. The prognosis in pink disease is good provided severe intercurrent infections do not supervene during the course of the disease, which lasts for several months. No local treatment of the ulcers is indicated.

Cancrum oris.—Also called noma and gangrenous stomatitis, this terrible disease has become very rare in this country owing to the improvement in social and nutritional standards. Rapidly spreading gangrene which begins on the cheek or gums causes extensive destruction and sloughing of the tissues of the face. The condition is probably basically nutritional and only occurs when the general resistance is greatly lowered. More than half of the reported cases have occurred in the course of measles or typhoid fever. The mortality is about 75 per cent.

TRAUMATIC ULCERATION OF THE MOUTH AND TONGUE

Palatal ulceration in infancy.—"Bednar's apthæ" are superficial ulcers which are seen in the early days of life or during the first few months. They are usually situated in the midline near the junction of the hard and soft palates. In the newborn the aspiration of mucus with a rough-edged aspirator at birth, or trauma with a finger nail when unnecessarily cleansing the mouth, is the chief cause. In older infants, in whom they are usually bilateral and may join a median ulcer, they are often produced by the friction of a rough hard teat or by too vigorous cleansing of the mouth. There is little inflammation and the lesions are shallow. They usually heal within a week but may be rather obstinate and interfere with comfort in feeding.

Treatment is mainly prophylactic; infants' mouths should be sacrosanct and cleansing should be deprecated.

Dental ulcers.—The sharp edge of a broken or carious tooth may cause ulceration of tongue or cheek, but this is uncommon in childhood.

Foreign bodies.—Sharp and rough objects, such as the end of a stick, may ulcerate the mouth during play. The palate is the most common site of these injuries, which are usually produced when a child with such an object in the mouth falls forward.

Whooping-cough.—In severe cases characteristic small ulcers are often produced on each side of the frænum linguæ by the lower incisors. They are of diagnostic value.

Corrosives.—Buccal ulceration may be produced by drinking or eating corrosive substances, such as acids or alkalis, if such dangerous substances are left within the reach of children.

OTHER CAUSES OF ULCERATION OF THE MOUTH AND TONGUE

Drugs.—Sensitivity to certain drugs, such as aspirin, may cause ulceration of the mouth, but this is uncommon. The application of gentian violet to the mouth in young infants more often than twice a day is liable to cause superficial sloughing and ulceration, particularly of the lower aspect of the tongue. The prolonged administration of mercurial preparations and of bismuth may cause ulceration which is characteristically gingival and situated behind the last molars. The new anti-folic acid drug, "aminopterin," which is being tested in leukæmia, produces vesicles with ulceration, particularly on the inner aspects of the lips, within a few days of its institution.

Allergy.—Some allergic individuals have repeated attacks of vesicles in the mouth. The lesions cease to develop with the withdrawal of food to which the child is sensitive. It is difficult to assess the frequency of allergic ulceration, but some believe that it is not uncommon.

Leukæmia.—Ulceration in the mouth tends to occur in advanced cases of acute lymphatic leukæmia in childhood.

Agranulocytosis.—Ulceration of the throat is likely to spread to the fauces and palate in severe cases of this disease. The possible value of a leucocyte count should not be overlooked in cases of obscure ulceration, particularly if certain drugs are being administered which may have a toxic action on the bone marrow.

THE BICENTENARY OF JOHN SIMS, M.D., F.R.S.

By LAURENCE DOPSON

It is strange that so little should have been written about John Sims, M.D., F.R.S., who was born 200 years ago, and that nothing, apparently, is to be found in medical journals, for Sims was a distinguished consultant, specializing in midwifery, as well as being a famous botanist and editor. A fairly full account of his life is given by Joseph J. Green in a paper "A Quaker Medical Trio named Sims and some account of that Family", which appeared in the *Friends' Quarterly Examiner*, 1913, p. 265. He should not be confused with John Sims (1792-1838), the pathologist, nor with James Sims (1741-1820).

The Sims's were a well-known Quaker family, who had mostly been tradespeople of some kind and who had suffered for their faith. The first of them to take up medicine was John's father, R. C. Sims, who graduated at Edinburgh in 1744, the title of his thesis being *De vomica pulmonis;* he practised for many years at Dunmow in Essex, where his surgery could be seen at least up to the 1914-18 war.

EARLY DAYS

John Sims, the only son of Dr. R. C. Sims, was born in the parish of St. Mary Bredman, Canterbury, on October 13, 1749. He was educated at home and at the famous Quaker academy at Burford, near Oxford, kept by Thomas Huntley, an ancestor of the Huntley of Huntley and Palmers, the biscuit manufacturer. In 1770, when he was twenty-one, John Sims went to his father's old university to study medicine. He remained at Edinburgh until 1773, going to Leyden for the session 1773-4. Returning to Edinburgh in the latter year, he was admitted to the degree of doctor of medicine on September 12, 1774. The title of his thesis was *De usu aquæ frigidæ interno* (Edinburgh, 1774) and he dedicated it not to one of the famous Edinburgh professors

Fig. 1.—John Sims (1749-1831), M.D., F.R.S., physician and botanist. From an engraving in the Wellcome Historical Medical Museum.

(as many candidates did, from motives perhaps not always dissociated from hopes for the results), but to John Fothergill, the famous Quaker physician. Among the points which Sims made in his thesis were that a moderate drink of water, by extending the muscles of the stomach, improved their tone, and that cold water, owing to its quality of being a fluid, cleansed the digestive passages and dissolved and carried away waste materials. He discussed its use in various forms of illness.

LIFE IN LONDON

In 1779 Sims came to London and bought the practise of Thomas Cogan (1736-1818), of Paternoster Row. The fact that he acquired this particular practise indicates that he had already decided upon his specialty, for Cogan, a founder of the Royal Humane Society who had been a clergyman but took up medicine at the instigation of his prospective father-in-law, was primarily an accoucheur. Sims was admitted a Licentiate of the Royal College of Physicians of London on June 25, 1779, but although he became a leading obstetrical physician, he was not among the ten who were granted the licentiateship in midwifery by the College.

Sims was appointed physician to the Surrey Dispensary and to the Charity for Delivering Poor Married Women in their own Houses. The former was established in 1777 and was then at Southwark. Physicians holding consultations had the right of having their pupils in attendance; instruction was also given there to midwives. The Dispensary's activities were not confined to midwifery, and an early medical communication by Sims, published in 1784, is an account of a 40-year-old serjeant of the Middlesex Militia who died at the Dispensary from cancer of the stomach. The Surrey Dispensary was the earliest appointment which Sims held in London. It was some years later that he succeeded Cogan as one of the three physicians to the Charity for Delivering Poor Married Women in their own Houses. This organization had as its treasurer and dispenser Mr. Peter Sharp, chemist and druggist, of Bishopsgate Without; founded in 1760, it should not be confused with the similar Benevolent Institution for Delivering Poor Married Women in their own Habitations, started in 1779. A Fellow, one-time President, and for many years member of council, of the Medical Society of London, Sims was a member of the Society's Midwifery Committee.

Another facet of Sims' professional activities is shown by his being made the first consulting physician to the Royal Ear Dispensary, which was founded by Dr. John Harrison Curtis (1778-1856) at Carlisle Street in 1816, and was later moved to 10 Dean Street, Soho; it was under the patronage of the Prince Regent, and in 1904 was rebuilt as the Royal Ear Hospital at 42-3 Dean Street.

SOME PRIVATE PATIENTS

Dr. Sims had a number of distinguished private patients; one of them was

Mrs. Fothergill, wife of Dr. William Fothergill. He was the regular medical attendant upon John Henton Tritton, another distinguished Quaker, and his family; in 1791 Sims was paid an extra five guineas for inoculating John, one of the sons. Tritton was Sims' cousin and paid him an annual honorarium for his attendances. In her journal under date "Mildred's Court, Eleventh Month, 25th", 1802, quoted in her "Life" by Susanna Corder (London, 1853), Mrs. Elizabeth Fry wrote: "My cough has been so poorly that my husband called in Dr. Simms. I asked his advice about our one (their eldest daughter, born in August, 1801) being inoculated, he strongly recommended the cow-pox, and said he would undertake the care of her if we liked; I think highly of his judgement, and I believe it is our duty to avoid evil, both bodily and mentally".

It has been stated that Sims at first opposed vaccination, but later became convinced of its efficacy. Perhaps it would be more accurate to say that he adopted a cautious attitude towards it in the beginning. In a communication to the *Medical and Physical Journal* early in 1799, he said the facts and experiments of Jenner certainly called for careful inquiry, but he felt doctors should hesitate before recommending the introduction on a large scale of "a hitherto nearly unknown disease" and warned about "rash experiments upon our fellow creatures".

> "If such hazardous experiments be not discouraged, there is some reason to fear that to the opprobium, the profession already lies under, of not being able to cure many of the existing diseases, will be added, that of having introduced new ones".

An editorial comment recognized the importance of the issues raised by pointing out: "From the above general statement, our readers will perceive that the great question respecting the utility of the cow-pox is at issue before the public". In a subsequent letter, however, Sims clarified his position:—

> "I had no intention of declaring myself an enemy to the inoculation of this disease; my only wish was, to induce practitioners to pause a little, to obtain more experience of its utility, before it should be *generally* recommended".

Later he admitted:—

> ". . . It must be acknowledged, that the experiments already instituted seem sufficient to decide that the cow-pox matter which has been used for inoculation is effectual in preserving the patient from any further attack of the small-pox, unless it should be true, which I deem very improbable, that cow-pox enables the constitution to resist the contagion of the small-pox for a certain length of time only."

It is an interesting indication of Sims' status that an editorial note to the first of these communications said: "The signature of the following communication . . . renders any introductory observations unnecessary".

There are two other references to Sims' private patients. One is in a letter by William Miller, another Quaker: "J. Wigham Tertius is under the care of Dr. Sims, who has advised him not to sit more than one meeting daily". Another is in the *Memoirs of Samuel Hoare*, also a distinguished Quaker. In 1798 Hoare was seized by a nervous affection. "Dr. Sims, his

old friend, attended him, and Dr. Reynolds was called in". A trip to Bath was advised.

Sims was called into consultation in two celebrated obstetrical cases—those of Joanna Southcott and of the Princess Charlotte.

THE CASE OF JOANNA SOUTHCOTT

Joanna Southcott was a queer woman, born in Devonshire in 1750 who considered herself in the rôle of a latter-day prophetess. In 1792 she announced herself to be the woman referred to in Revelations, Chapter XII. In her "Third Book of Wonders" (London, 1814) Joanna again announced "the coming of Shiloh", declaring that "The Spirit" had told her: "This year, in the sixty-fifth year of thy age, thou shalt have a son by the Power of the Most High". Although she had ceased menstruating many years previously, Joanna was now convinced that she was pregnant. Her followers believed her in this as in all things, and are said to have showered upon her such gifts as "a mohair mantle, which cost £150!!! splendid silver pap spoons, and a caudle cup (one shaped like a dove)" and "a magnificent Crib" which, "with its ornaments, decorations, bedding, &c. cost upwards of £200!!!"

Not only her followers but also her medical attendant, Dr. Richard Reece, had no doubt about the cause of Miss Southcott's symptoms being other than as she claimed. Correspondence on the matter began in the public press in August, 1814, and it was said that the medical attendants were satisfied that the prophetess was with child—or more specifically, with Shiloh. In view of this, Dr. Sims, to make clear his position and opinion, wrote a letter which was published in the *Morning Chronicle* of September 5: "Several persons having expressed a wish that I should visit Joanna Southcott, that they might be satisfied what foundation there was for a report that she was pregnant, [he wrote] I consented to accompany one of her friends, a surgeon and accoucheur of experience, for that purpose, on the 18th of August". He describes in detail the examination which he made and the condition of the breasts. "I proposed to put my finger upon the navel, without any covering, which was permitted. This part I found sunk in, not at all protruded as in pregnancy". He could feel no movements of the fœtus, although Joanna declared that she felt them clearly. Dr Sims gave his opinion as follows:—

> "Considering all the above appearances, I did not hesitate to declare it to be my opinion, that Joanna Southcott was not pregnant; but was told that I was the first medical man that had seen her that was not perfectly satisfied of the contrary.
>
> "I believe that her uterine organs are diseased, and that the breasts, as is usual, sympathyzing with those parts, have an increased quantity of blood determined to them".

He ended his letter with these words:—

> ". . . Yet, before I conclude, I feel it right to say, that I am convinced that this poor woman is no imposter, but that she labours under a strong mental delusion".

Nothing was thought in those days of medical men discussing such a matter in the public press, and this letter—the only one which he wrote during the controversy—shows that Sims was sufficiently highly regarded in his profession to be looked to for an authoritative opinion in a difficult case—a regard justified by his views in this instance—that he was a thorough clinical observer, and, as is evidenced by the concluding paragraph, a kindly man.

His letter brought an instant rejoinder from Dr. Reece, which the editor of the *Morning Chronicle* refused to publish; it was, however, published in the *Sunday Monitor and Sunday Review*. In it Reece sought to argue that Sims was wrong in his conclusions. It is noteworthy that although other medical men, including Professor Assalini, Professor of Midwifery in Paris, saw Joanna Southcott, none of them, except Sims, instantly recognized and were convinced of the non-existence of the pregnancy.

Although Dr. Reece came to recognize the error of his earlier view, he could not convince his patient. Joanna Southcott, still believing that she had within her the Shiloh, died on December 18. She gave instructions that her body should not be opened before four days had elapsed, being certain that the corpse would remain fresh and that she would return to it. When the post-mortem examination was held, however, the "disciples" who attended fortified themselves by smoking strong tobacco—"a proof that they did not consider the prophetess to possess the most savoury odour". The examination was conducted by Dr. Reece, in the presence of Dr. Sims and Mr. Mathias. The result of the examination showed: "first, that there was no Shiloh; next, that there was no disease of the uterine organs, as imagined by Dr. Sims; thirdly, that the uterus, instead of being enlarged, was remarkably reduced". The omentum was extremely large and appeared to be one lump of fat. "Dr. Sims having expressed a wish to examine the state of the breasts, to satisfy himself on this point [wrote Dr. Reece] I dissected one of them, which shewed the fullness to proceed from an enlargement of the mammary gland as I had stated, and not from accumulation of fat, according to his opinion". This remark of Dr. Reece's would reflect more to his credit and professional acumen had he not been so stubborn in denying for a long while Sims' opinion on the vital issue, whether there was or was not a pregnancy. The necropsy failed to establish any organic cause for Joanna's death.

The case naturally aroused great interest, but at least Dr. Sims emerged with dignity and without loss of respect. One account says:—

"Dr. Sims did not fawn on her when living, and vilify her when dead . . . Had the whole college of physicians been in attendance on her, a better understanding of her case, we take on us to say, from our professional knowledge, could not have been given. In the opinion Dr. Sims gave of herself and her state of body, he shewed the goodness of his heart as a man and a Christian. And, had all her attendants had the same penetration and integrity, she would have, in all probability, been delivered long before her death; not of a child, but of the delusion".

The danger of applying logic to medical matters is shown by the opinion expressed to Joanna by a lady who saw her after Dr. Sims had called, and assured her he was wrong: "I have had eleven children, and the objection he mentioned happened to me with every one of them", she told the prophetess hopefully.

DEATH OF THE PRINCESS CHARLOTTE

It is unfortunate that the other famous case in which Sims was called as a consultant also ended tragically. It was that of the Princess Charlotte. The Princess seems almost to have had a foreboding of what was to come, for a month before her confinement, she wrote a letter to her mother which contained such phrases as "I fear less to die than to live".

Sir Richard Croft, a colleague of Sims at the Surrey Dispensary, was in charge of her confinement, and three weeks before it was due to begin, he went down to Claremont to be with the Princess. What followed is detailed in the following memorandum (Royal Archives, Georgian Papers 50067), which His Majesty the King has been graciously pleased to allow me to reproduce for the first time:—

"The Labour of Her Royal Highness Princess Charlotte began at Seven oClock on Monday Evening the 3d of November 1817, and terminated at Nine oClock on Wednesday Evening the 5th of Novr, in the birth of a Still-born Male child—The Labour therefore continued during fifty hours—The exertions of the uterus were feeble throughout the greater part of the Labour, but during the last few hours were stronger, and more satisfactory—As the Labour was very tedious, Dr. Sims was sent for by Sir Richd Croft on Tuesday Evening, and arrived at Claremont about Two oClock on Wednesday morning—He concurr'd entirely in opinion with Sir Richd Croft respecting the situation of Her Royal Highness, and that as long as the Labour was making progress, altho' slowly, the conduct of it should be left to Nature—Instruments were at hand to assist the Uterus, if it were thought adviseable to employ them—During the whole of this tedious Labour, Her Royal Highness was cheerful, look'd well, and Her pulse was good—She often walked about the Rooms, and was very little on Her bed—

"The Child was born, as before mentioned, at Nine in the Evening, and as upon examination, an hour-Glass contraction of the Uterus was discover'd, Sir Richd Croft took away, with the concurrence of Dr. Sims, the afterbirth about twenty minutes before Ten—Her Royal Highness appear'd quite as well as women commonly do after so tedious a labour, and much better than they often do under such circumstances, till about a quarter before Twelve at night—Her Royal Highness then complained of some sickness and singing in Her Ears—Soon after this Her Royal Highness threw up from Her Stomach a little fluid, which seem'd chiefly some camphor mixture, which She had swallowed—She then became a little irritable, and began to talk somewhat too much—About a quarter before One Her Royal Highness complained of great uneasiness in Her Chest, and breathed with great difficulty: Her pulse was very feeble and irregular, and She became extremely restless, not being able to remain a single moment in the same posture—This very alarming state continued and kept increasing till half past Two in the morning, when Her Royal Highness expired—Her mind was entire throughout the whole of this dreadful attack—

The Child had been born dead, but appeared not to have been dead long—The most strenuous efforts were made to reanimate it by means which had been previously provided, but they were unavailing—Some circumstances had render'd it

probably that the Child would be still-born, and therefore every means of recovery were in readiness".

Novr 9—1817

M. Baillie
Richard Croft
Jn° Sims"

Such were the terrible sufferings of this girl of twenty-one. It was Sims who made the "most strenuous efforts" to revive the child. Sims added the following postscript to the memorandum:—

"As some of the above circumstances could not come under my immediate observation, not having seen her Royal Highness till symptoms of danger occurred, I beg leave to add, that on my arrival at Claremont, Sr. Richard Croft proposed to mention it to her Royal Highness and to introduce me; but as the state of the labour, at that time, precluded all thoughts of having recourse to any artificial assistance, both Dr. Baillie and myself thought that this was not only unnecessary but unadvisable. And as the labour continued from that time to the end progressive, there was no period of it, at which a question about the propriety of using instruments could have been entertained.—I was in the adjoining room the greater part of the day, and was continually informed of the state of the labour, and could have seen her Royal Highness, whenever it had been thought advisable. When it was found that the afterbirth did not come away favourably, I was perfectly satisfied with Sr Richard Croft's representation and quite agreed with him in the propriety of removing it. I was at that time still engaged in fruitless efforts to reanimate the child; and the introduction of a stranger, at that moment, to the royal patient, as it appears to me, was particularly objectionable.

Jn° Sims"

In the collection of manuscript letters and other material relating to Mathew Baillie, in the Library of the Royal College of Surgeons of England, the first part of the memorandum above, which is stated to have been "written for the satisfaction of the Royal Family", has been copied out by Mrs. Baillie. In this copy some parts of the original have been omitted and there are some textual variations, but the additional information is given that the child was perfectly formed and weighed nine pounds, whilst attached to the memorandum (on which only Baillie's signature is given) is the following note, stated to have been found in Baillie's own handwriting:—

"In looking back very often upon this most distressing event I am convinced that Sir Richard Croft did all that the melancholy case admitted of, and that the Princess Charlotte's life would not have been saved by any different treatment".

The controversy aroused by the death of the Princess was considerable. Although the Prince Regent assured Sir Richard that he was perfectly satisfied with his conduct, most blamed him for allowing the Princess to remain in labour for so long without attempting to terminate the birth. On February 13, 1818, Sir Richard Croft was found dead. He had shot himself.

Again it shows the regard in which Sims was held as an obstetrician that he should have been called in when complication arose and that he should so clearly have been appealed to by Sir Richard and Dr. Baillie as the superior authority. One account says of the summoning of Dr. Sims:—

"This, as a precautionary step, is honorable to Dr. Croft, and will ever shield him against a successful imputation of timerity".

Criticism has been raised against Sims because he did not go in to see the Princess, yet signed bulletins saying she was progressing favourably. "How this gentleman", declared Lady Anne Hamilton, "could allow his name to be thus affixed to a declaration, of the truth of which he was totally ignorant, we do not know, but the time-serving press said 'That Dr. Sims being unknown to the Princess, his appearance in her chamber might have alarmed her' ". As has been seen, it was Sims himself who took this view, which was thus not an invention of the newspapers—and she also rather destroys her case by being too violent and accuses Croft of having poisoned the Princess on instructions.

Sims, with Baillie and Croft, followed the remains of the Princess to her grave at St. George's Chapel, Windsor. One wonders whether the outcome of the whole affair might have been happier had Sims been summoned earlier. As it was, this tragedy brought about the reign of Queen Victoria.

LITERARY WORK

At the same time as he was involved in these two important midwifery cases, which show that he was actively engaged in practice, Sims was editing the celebrated *Botanical Magazine*. He became editor soon after the death in 1799 of William Curtis, the founder editor, although his name first appeared on the title page in 1801. That the editorship of a leading scientific journal of this kind, the circulation of which exceeded 3000, was no sinecure can well be imagined, and is shown in the correspondence in connexion with it preserved at the Library at Kew Gardens, and in letters by Sims in the manuscript collections at the Botanical Library of the Natural History Museum and the Linnæan Society of London. It is interesting to note from these letters that Sims in no way rose above the failings, or perhaps one should say had to contend with the same difficulties, as other editors of recent times, for one finds queries about what has happened to material sent for publication and when such-and-such note will appear. An editor, particularly of a scientific magazine, has to be tactful. In a letter dated November 26, 1806, and quoted by courtesy of the Director of Botany, British Museum, Sims told Mr. Robert Brown, an eminent botanist, that people who sent new flowers to be drawn were apt to be offended if these did not appear fairly soon and would at another time send them to a rival journal: "In order not to give offence in this way I am often in some degree obliged to publish drawings, which I otherwise wish to delay". In another letter (to Dr. William Swainson, dated May 8, 1820, now in the possession of the Linnæan Society) Sims points out that as he is personally responsible for the nomenclature and the accuracy of the drawings, he may wish to see actual specimens, as well as drawings. As editor, Sims had his troubles also in respect of the circulation of his magazine. From the 172nd issue he increased the number of plates in each part to four, and later he increased the number to eight and the price to 3s. 6d. The rise in price and the

appearance of rival journals led to an immediate drop in circulation, sales falling by a half and later by more still. It was a grim prospect, but ultimately the *Botanical Magazine* weathered the storm, and its publication continues to-day, having been uninterrupted since 1799.

Sims undertook the editorship under the will of William Curtis, whose friend he had been for many years—probably they were schoolfellows together. Mr. W. Hugh Curtis, in his book "William Curtis, 1746-1799" (Winchester, 1941), explains that Curtis made Sims one of his executors; as such Sims's name appears in an agreement of January 16, 1815, by which George Graves became part owner of William Curtis's *Flora Londinensis*. In addition to the *Botanical Magazine*, Sims also edited, with Charles König, the *Annals of Botany*, of which two volumes only were published (London, 1805 and 1806); it is an interesting publication which includes historical articles. The combination of an expert interest in botanical matters with a medical practice was quite common at this time: John Coakley Lettsom, founder of the Medical Society of London, had a botanical garden at his country house at Camberwell. and it was he who introduced the mangel wurzel; whilst John Fothergill formed a large botanical garden at Upton. Sims probably inherited his interest in botany from his father, who was passionately fond of gardening.

No source that I have discovered has any details of Sims' medical publications; the *Surgeon General's Catalogue* only gives his degree thesis. He did, however, communicate a number of papers on medical matters, and a list of the ones which I have been able to find is given in an appendix to this article. In addition, Sims probably wrote the biography of William Curtis in the *Gentleman's Magazine*, 1799; it is said that Curtis left Sims the memoirs of his life. Sims delivered the Oration to the Medical Society of London during his year as President (1783), but this does not seem to have been published. A list of his botanical papers appears in J. Britten and G. S. Boulger's *Biographical Index*.

PERSONAL LIFE

Not a great deal is known about Sims' personal life. He married about 1790, and because his wife was not a member of the Society of Friends, he was compelled, under the rule then existing, to leave the Society. The same choice between love and creed had to be made by Lord Lister, when he had to leave the Quakers on marrying Agnes Syme, who was an Episcopalian. Sims, however, continued to move in Quaker circles and, as we have seen, many distinguished members of this sect were his patients. William Miller's letter of 1821 refers to Sims having "lately laid aside his cockt hat"; this may mean that he had been rather more ostentatious in his dress than strict members of the Society could altogether approve and that he was now adopting or reverting to the more severe style of dress. That he was a "clubbable" man is shown by his membership of societies of medical men,

whose meetings were more convivial affairs in those pre-Bevan, pre-Strachey days. The Society of Physicians, for example, of which select group he was a member, met "once a fortnight, on Wednesdays in the evening, at Old Slaughter's Coffee-house, for the purpose of conversing on the prevailing diseases, &c. and once a quarter they dined together at the Crown and Anchor Tavern in the Strand"; Old Slaughter's Coffee House seems to have been a favourite place for medical gatherings, for the Society for the Improvement of Medical Knowledge, founded in 1782, "for the purpose of collecting useful essays and observations for publication", also met there once a fortnight, with Sims among the company, and this Society, too, had its quarterly dinners.

John Sims was a founder member of the Linnæan Society of London, and in 1816 he presented to the Library of this Society a particularly fine edition of Leonhard Fuchs' *De historica stirpium commentarii isignes* (Basle, 1542). He was admitted a Fellow of the Royal Society in 1814.

Sims was very early interested in the idea of forming a Society for Relief of Widows and Orphans of Medical Men, taking part in the early meetings in 1788 in connexion with it; his name appeared in the first advertisement as one of the four treasurers. In September, 1807, the Society had been experiencing difficulty in getting together a sufficient number of directors to transact business. Mr. James Ware, one of the Vice-Presidents, conceived that they might be more likely to come at the appointed hour if their fares were guaranteed, and he gave £100 of Navy 5 per cent. stock for this purpose; the Society doubled the amount, and Dr. Sims gave £10 also.

There is a rather quaint glimpse of the domestic life of John Sims in a reference in his paper on the use of pure ammonia in pregnancy (1799):—

"I was first led by accident to the discovery of the extraordinary power of the pure ammonia in correcting acidity in the stomach, over other alkaline substances. My wife being seized one night with a severe heart-burn, I arose with a view of getting her some magnesia; but not being able to find any, and being desirous of procuring her some immediate relief, I expected to obtain this by any alkaline substance, and not meeting with any but the water of pure ammonia, which I happened to have by me, I administered twenty drops in a glass of water; the relief was instant and more complete than she had ever experienced from taking magnesia".

Ann Sims was seven years younger than her husband. She bore him six children, four girls and two boys. One of the boys died in infancy; the other graduated M.B. at Cambridge in 1810 and became M.D. of that University in 1823. It is significant that Sims, the fashionable London physician, sent his son to one of the old universities in England and not to his *alma mater;* and further, that when this son, having qualified as a doctor, forsook medicine for religion, he should become a priest in the established Church of England. In a letter dated Dorking, September 3, 1828, John Sims writes of this son:—

"Courthope goes on preaching &c at two parishes every Sunday and goes through the duties of his profession *con amore*. It seems to suit him much better than the one he has deserted".

The letter adds that Courthope would soon be going to Fittleworth, "for which parish he was originally ordained". Green states that he became Rector of Petworth, also in Sussex, and died at Undercliffe, Isle of Wight. The present Rector of Petworth, Rev. Harold Godwin, informs me, however, that Courthope Sims' name does not appear in the official list of rectors. Courthope was, however, curate at Fittleworth between 1829-32; the first funeral he took there was on December 19, 1829, and the last on April 4, 1832. His own burial entry gives his age as thirty-eight, and his abode at the time of death as Ventnor.

Incomplete lists of Sims' London addresses have been given, but the following, supplemented by reference to original letters, is the full number: Paternoster Row; 31 New Bridge Street, Blackfriars; 67 Upper Guilford Street, Bloomsbury; 37 Wimpole Street.

One of the Kew letters must have caused Sims a little misgiving as he read it, for the writer, Thomas Guest of Sierra Leone, announces his intention of sending to England "a monstrous great Pelican".

> "The Fellow is quite tame, and I hope to preserve him during the rains: He eats Fish, Flesh, Fowl, or any thing that comes in his Way; he devours a great Deal, and I am sometimes very much puzzled to get victuals for him. I suffer him to stroll about, and he is become the Terror of all the Women & Children in the Colony; if any of them are going by with Meat or Fish, and he sees them, he is after them immediately, and ten to one but he gets it".

However, Guest hastens to add:—

> "I am aware you cannot keep him in Bridge Street, but I think among your Friends, there are some who would be glad to have such a Bird. Sr Joseph Banks probably".

These letters to John Sims show that in connexion with the *Botanical Magazine* he carried on a correspondence with people in all parts of the world. They also show that he could write shorthand. Several letters contain endorsements by Sims in shorthand, and one of the letters, from William Grover (21 February, 1825), states:—

> "My dear friend,
> Enclosed I hope thee wilt receive safe the System of Shorthand, as proposed".

I have submitted some copied examples of John Sims' shorthand to Mr. William J. Carlton, an expert on the history of shorthand, but unfortunately they were too fragmentary for him to identify. It was, however, definitely not Byrom's or Taylor's (two of the most popular pre-Pitman systems). It is also impossible to identify the "System of Shorthand" referred to by Grover, but if it was a different system from the one that Sims was using, it cannot have impressed him, for apparently he continued with the same outlines. It does appear that the shorthand which John Sims wrote was the same as that used by William Curtis, of which an example is illustrated in W. Hugh Curtis's book, but Mr. Carlton warns me that the

shorthand systems of this period often bear a superficial resemblance to each other.

CLOSING YEARS

The letters at Kew concern the *Botanical Magazine*, and when they are from medical men, make no mention of purely medical matters. The letters from William Fothergill, however, give some interesting glimpses of the life in retirement of this physician and of his interests:—

Carr End, Yorkshire. February 26, 1819.

"My dear Wife has for several months, been nearly quite confined to her room, yet on the whole she is something better, and I hope will again be restored to her usual share of health when that season arrives, inspiring 'Vernal delight & Joy'.

"We have had the finest autumn and winter hitherto, I ever remember. Our little garden has never been without a variety of flowers, & we are at this moment quite gay with a profusion of crocus's, winter aconites &c . . . During the time you were enveloped in cold gloomy fogs, we were enjoying bright sunny days, and the frost quite moderate".

A letter of October 30, 1826, tells of the arrival of a number of issues of the *Botanical Magazine*:—

"which indeed is to me & my wife and daughters a high treat; lock'd up as we now are in all the rigour of winter, we are enjoying the beauties of Flora, while sitting at our Fire-side. . . . My own health as well as that of my wife (thy old patient) continue much as when I wrote last, but the hand of time is upon us, and we must expect to feel the effects of increased years. I have recently entered upon my 78 year, & I hope I am endeavouring to be thankful that my infirmities are not more and greater".

In 1826, at the age of 77, John Sims resigned the editorship of the *Botanical Magazine*. He retired to Dorking, in Surrey. In a letter which he wrote from there to König on March 4, 1829, and which is now at the Natural History Museum, it appears that there was a question of his herbarium and library going to the new London University.

"What occurs to me as the best plan of disposing of my library and herbarium would be to submit it to a valuation and if the London University will agree to be the purchaser I will consent to deduct a fourth part of the price at which it may be valued.

"My library consists of most of the old botanical authors but not many of the expensive coloured works in a perfect state . . . "

The offer evidently fell through, for the library and herbarium were sold by auction by Mr. Thomas "at his Great Room, 38 King Street, Covent Garden, on Tuesday, May 26th, 1829, and following day, at Twelve for One o'Clock very punctually". The catalogue of the sale, a copy of which is at the Natural History Museum, lists 722 lots and states that in addition to the "choice Botanical Library" the collection included "a small misscellaneous Library, in which will be found Fowler's mosaic pavements, and a variety of Works of the best modern Authors". The herbarium is now at Kew.

In a letter to Alexander McLeay, on the latter's departure in 1825 to be colonial secretary in New South Wales, it is evident that Sims had become rather aware of the declining years, for he writes:—

"I am very sorry we are like to lose you soon and at my time of life I can hardly expect to live to see you on your return".

When he went to Dorking, the effect of the three score years and ten was upon him, as is rather pathetically borne out by two passages in letters to his friend Charles König. The first is dated Dorking, September 3, 1828:—

" . . . It would give me particular pleasure to see you, but I grow so feeble that I am able to go but a very little way from home and much question if I shall ever be again equal to undertake a journey to London, though I hardly like to think so, as I much wish to get another sight of some old friends, of which you stand among the foremost. I thank God my eyesight continues pretty good and I find amusement in reading; but writing has become difficult . . . "

Despite the difficulty in writing, of which he complains, this letter is in his own hand and the words are firm and clear. A few months later, however, he had evidently got past writing altogether, for the next letter, dated Cotmandene, Wednesday, March 4, 1829, has been dictated and is written out by another. In it, Sims says:—

"Mrs. Sims and my family are all in pretty good health and as to myself I have little to complain of but an increasing debility which is now so great it is not at all probable I shall be able to go to London again so that I shall feel the more gratified by any occasional visits from my friends".

It is probable that Sims chose his place of retirement to benefit his failing health. Of the situation of Cotmandene, a guide book of 1865 says:—

"This emminence overlooks the Town and embraces views of Denbies, Box Hill, Norbury Park House, and Camilla Lacey. This elevation has long been proverbial for the superiority of its situation, and the air is fresh, breezy and healthful".

Another guide book also describes it as "one of the healthiest parts of the town".

It was in this pleasant spot that John Sims, M.D., F.R.S., died, in his 82nd year, on February 26, 1831.

Surprisingly, very little attention seems to have been paid to his passing, and only brief notices appeared in the *Gentleman's Magazine* and *Annual Register*, and none in *The Times* or the *Lancet*. Previously the place of burial of John Sims has been a mystery. Green stated he could find no indication of where either John Sims or Mrs. Sims was buried. The Vicar of Dorking, Rev. K. D. Evans, kindly searched the Register at Dorking for me without result.

In fact, John Sims was buried on March 5, 1831, at Fittleworth in Sussex, where his son Courthope was curate. The service was conducted by the Rev. Robert Tredcroft, the incumbent, who was at this date styled vicar. It was in the same churchyard that Courthope Sims was buried on November 8, 1833. Green states that Courthope's widowed mother died at

the Rectory House, Petworth, shortly after her son's death, on April 19, 1835, and there is a record of the burial at Fittleworth of Ann Sims "from Petworth" on April 28, 1835. She was aged 79 and the burial was conducted by Rev. C. Dyson, curate. I am indebted to Rev. J. E. Dieterlé, Rector of Fittleworth, for this information.

FIG. 2.—The church of St. Mary the Virgin, Fittleworth. In this Sussex church, where his son, Rev. Courthope Sims, M.D., was curate, the burial service of John Sims, M.D., F.R.S., was held. Under an old yew tree in the churchyard are buried John Sims, his wife Ann, and his son Courthope.

John Sims was at least not unremembered by his botanical friends. Robert Brown commemorated his name in the Mexican genus of compositæ *Simsia;* he is also commemorated by the plant *Simsia amplexicaulis*.

The only memorial to the Sims family is a small stone surmounted by a Maltese cross. It stands under the old yew tree in Fittleworth churchyard, and on it can be read just this:—

J.S. M.D. 1831
C.S. M.D. 1833
A.S. 1835

On either side of this headstone are two others, small, overgrown, and nearly buried in the earth until the Rev. J. E. Dieterlé had them dug out. One proved to be the headstone of Courthope Sims and is broken, which may indicate that the stones were shifted when the nave was taken down in 1871. The other is inscribed:—

I S
Born 10th Novr
1749
Died 26th Feby
1831

APPENDIX I

Medical Papers by John Sims

The following are the signed medical papers or communications by John Sims the publication of which I have been able to trace; the general index to the first volumes of the *Medical and Physical Journal* wrongly lists his contributions under the name of James Sims, whilst the paper read to the Medical Society of London in 1788 on "A passage from the Ancient Greek authors on Hydrophobia" by a "Dr. Sims", which Green thought might be by James or John Sims, was read by the former.

"An account of a cancerous affection of the stomach". *Medical Communications* 1782-4 (1784), **1**, p. 421.

"Letter on the Cow-Pox". *Medical and Physical Journal* (1799), **1**, p. 11.

Further letter on the same subject. *Ibid.*, p. 230.

"On the use of pure ammonia in pregnancy". *Medical and Physical Journal* (1799), **2**, p. 205.

"On the Cæsarean operation". *Ibid.*, p. 433.

"An account of a ruptured uterus". *Medical Facts and Observations* (1800), **8**, p. 150. Report and extracts of this paper are given in *London Medical Review* (1800), **3**, p. 372.

"On delivery in certain difficult cases of arm presentation". *Medical and Physical Journal* (1802), **8**, p. 481.

In addition, Sims communicated to the Society of Physicians "An account of expoliation of the internal surface of the tibia, removed by the application of the trephine" by Mr. Thomas Whateley, *Medical Communications* (1790), **2**, p. 386, whilst a paper by Mr. Whateley ("Cases of prolapsus uteri") contains an account of a support for a case of prolapsus uteri, designed by Dr. Sims (*Medical Facts and Observations* (1800), **8**, p. 172).

Sims' botanical papers are listed in J. Britten and G. S. Boulger's *Biographical index of deceased British and Irish botanists* (2nd edition, London, 1931).

APPENDIX II

Manuscripts of John Sims

The following list is given to supplement the incomplete reference in Britten and Boulger:—

Natural History Museum, British Museum. The Botanical Library possesses four letters, three by Sims and one to him.

Linnæan Society of London possesses two letters by Sims.

Kew Gardens library has a collection of letters to Sims, but not by him, and also notes of a botanical paper.

Permission to quote from these letters is gratefully acknowledged.

CURRENT THERAPEUTICS

XXVI.—BLOOD TRANSFUSION AND BLOOD SUBSTITUTES

By GEOFFREY H. TOVEY, M.D.

Director, South-West Regional Transfusion Service; Clinical Teacher in Hæmatology, University of Bristol.

THE past ten years have seen a great increase in the therapeutic use of blood and blood substitutes. This increase has arisen mainly because of the development of the blood bank system, which has simplified the technique of blood transfusion both for the doctor and for the blood donor.

The blood bank was first conceived and operated by Captain O. H. Robertson, R.A.M.C., in a British Casualty Clearing Station in France in 1917, but its principle was not applied on a large scale in Great Britain until 1940, when blood banks were organized for the treatment of air-raid casualties. War-time experience of the transfusion of preserved blood and the advantages of the blood bank system led to the inception of a National Blood Transfusion Service in 1946.

PRESERVATION OF BLOOD

It has always been apparent that the technique of transfusion would be greatly simplified were it possible to store blood for an extended period. This would enable blood to be collected at a convenient time and to be available for emergency use. It would further give sufficient time for grouping and cross-matching, thus increasing the margin of safety. Satisfactory preservation of red cells was attained eventually by the addition to the citrate anticoagulant of sufficient dextrose to secure a final concentration of 0.5 per cent., the adjustment of plasma pH to 7.1 to 7.3, an optimal dilution, and storage at a constant temperature of between 2° and 6° C. In practice, these standards are achieved by collecting blood into an acid-citrate-dextrose mixture (A.C.D.*) at the rate of 120 ml. of A.C.D. to each 440 ml. of blood, and storing in an adequately supervised blood-bank refrigerator. Stored in this way for up to 21 days, the blood is as effective as fresh blood in cases of hæmorrhage for blood volume restoration, and in cases of anæmia the transfused red cells show practically the same survival in the patient's circulation as those of freshly drawn blood. The vast majority of transfusions are given for one or other of these reasons.

Whole blood cannot be sterilized and any chance bacterial contaminants are prevented from multiplying only if the temperature of the blood is kept constantly below 6° C. Bacterial growth may convert a life-saving fluid into a highly toxic one, and it is vitally important that blood be kept at the

* Disodium citrate, 2 per cent., 100 ml.; dextrose solution, 15 per cent., 20 ml.

correct temperature until just before transfusion. During storage the red cells sediment rapidly leaving an upper layer of straw-coloured plasma which can be utilized as a convenient indicator of fitness for use. Bacterial multiplication will generally result in hæmolysis of red cells, so that the liberated hæmoglobin pigment diffuses into the supernatant plasma. A bottle of blood must not be transfused therefore if it shows any pink or red staining in the plasma.

Hæmolysis is not, however, an infallible safeguard, and some bacilli can multiply at refrigerator temperature if they have previously been stimulated by exposure to a higher temperature. These organisms cause only slow hæmolysis, and it is therefore possible for a bottle of stored blood to be heavily infected without showing hæmolysis. This may happen when a bottle is taken from the refrigerator and returned after being exposed to room temperature for a few hours. The only adequate safeguard in the prevention of tragedies from this cause is continuous and accurate refrigeration. Blood taken from a refrigerator for more than 30 minutes and allowed to warm up should on no account be restored to the refrigerator for use on a future occasion. Storage of blood below 2° C. is contraindicated because of the danger of damage to the corpuscles from freezing.

After 21 to 28 days' storage, the red cells become increasingly fragile and should not be transfused. The supernatant plasma is stable and may be decanted and prepared for transfusion as a blood substitute.

INDICATIONS FOR TRANSFUSION VOLUME AND RATE

Transfusion of blood is indicated principally in patients with hæmorrhage and in cases of anæmia. Less frequently blood is transfused to cases of hæmorrhagic diathesis, infective states, agranulocytosis, and to patients with protein deficiency.

Acute hæmorrhage.—The average adult will react unfavourably to an acute blood loss of more than two pints. Transfusion is indicated therefore whenever the loss has been of this magnitude, or as a prophylactic measure during operation should such a loss be anticipated. The extent of the hæmorrhage may readily be assessed if the bleeding is external and the blood is collected. This is generally possible in a case of obstetrical hæmorrhage. When the blood has not been saved, or bleeding is internal, an estimate must be made from the clinical signs of reduction in circulating blood volume. These include pallor, tachycardia, sweating, vomiting and, in most instances, a fall in blood pressure.

Patients who have been severely injured or who have obviously suffered gross blood loss require immediate transfusion regardless of blood pressure, and those in whom the systolic pressure has already reached a figure of 80 mm. Hg or less likewise brook no delay. In less severe cases the blood

pressure should be estimated every ten to fifteen minutes. Transfusion will be indicated if the systolic blood pressure is obviously declining or if it remains below 100 mm. Hg for one hour. Compatible whole blood should be transfused as rapidly as possible (one pint every five to ten minutes) until the systolic pressure is 100 mm. Hg. Thereafter, as the blood pressure reaches its normal level, and there is a general clinical improvement, the transfusion is slowed from a rapid drip rate to 40 drops per minute. Restoration of circulating blood volume must be rapid, or irreversible changes may take place in the brain, leading to blindness or death, or in the kidneys, resulting in renal impairment or renal failure.

The anæmias.—Blood is transfused to patients with anæmia to provide oxygen-carrying red cells, and will be required: (a) when red cell deficiency is so severe as to constitute an immediate threat to life, e.g. hæmoglobin below 20 per cent. (2.9 g.); (b) in the aplastic and refractory anæmias; (c) in hæmolytic anæmias; (d) in cases of dyshæmopoiesis complicated by infection, when hæmatinics such as iron, liver or vitamin B_{12} are temporarily ineffective; (e) as a preoperative measure.

Because of the necessity for red cell replacement, the fluid of choice is a *concentrated red cell suspension.* Such preparations may be obtained, following twenty-four hours' notice, from the regional transfusion centres and from many large hospitals. They consist of the red cells of two bottles of whole blood suspended in a minimal volume of plasma*. The amount to be given depends upon the extent to which the hæmoglobin is to be raised. One pint of whole blood will raise the hæmoglobin by 6 to 7 per cent., and one pint of concentrated red cells by 12 to 14 per cent. The drip rate should not exceed 40 drops per minute (or 60 drops per minute if a single bottle only is to be given), and not more than two bottles should be transfused in any one period of twenty-four hours. When more than two bottles are needed to increase the patient's hæmoglobin to a sufficient level, an interval of at least twenty-four hours should be allowed between each transfusion for circulatory readjustment.

Among the body's compensating measures in a severe anæmia are a marked reduction in total blood volume, an increased cardiac output, and an increase in right auricular venous pressure. This latter is reflected in engorgement of the neck veins. When the hæmoglobin is below 30 per cent. the anæmia has been long standing, or, in a case of chronic sepsis, the myocardium is impaired, and transfusion must be given with the utmost caution. The initial transfusion should be limited to one half-pint of red cell concentrate at a drip rate of 10 to 15 drops per minute. The patient is

* In emergency, a concentrated red cell suspension may conveniently be transfused by introducing a giving set into a bottle of ordinary stored blood without disturbing the red cell sediment at the bottom. The bottle may then be slowly and carefully inverted so that the red cells come to lie in the neck and are transfused in a minimal volume of plasma.

exposed to a grave risk of cardiac failure should the transfusion be accompanied by a rigor.

Hæmorrhagic diatheses.—Transfusions of whole blood are given to provide defective clotting factors (in hæmorrhagic disease of the newborn, prothrombin; in thrombocytopenic purpura, platelets; in hæmophilia, thromboplastinogen) and to replace blood lost. In severe cases of *agranulocytosis* whole blood is transfused to provide leucocytes. White blood cells and essential clotting factors deteriorate rapidly during storage, so that blood transfused to supply these elements must be fresh.

Infective states and protein deficiency.—Hæmoglobin synthesis has a prior call upon available protein. In infective states or protein deficiency it is necessary therefore to correct any existing anæmia by transfusing concentrated red cells or whole blood before protein can be utilized by the body for tissue protein or antibody synthesis.

Exsanguination transfusion.—Withdrawal of the patient's blood and simultaneous replacement by suitable donor blood is practised in hæmolytic disease of the newborn, acute leukæmia, and some types of acute poisoning. In hæmolytic disease of the newborn a plastic catheter, 0.1 to 0.2 mm. bore, is passed *via* the umbilical vein into the inferior vena cava, and the blood is exchanged by syringe, 10 to 20 ml. at a time, until at least 60 ml. per pound body weight have been replaced. Insufficient information is as yet available to determine whether or not this procedure is more effective than simple transfusion.

In 1947, Bessis and Bernard reported striking remissions in certain cases of acute leukæmia following complete blood replacement. No further reports have appeared in support of these claims, however, and results in Britain with this treatment have not been encouraging.

COMPLICATIONS OF BLOOD TRANSFUSION

If scrupulous attention is paid to detail, the majority of transfusions of whole blood or packed cells can be free from complication.

The most frequent complication is the *pyrexial reaction*, which in its most severe form presents as a rigor. Such reactions are usually due to imperfectly prepared transfusion materials and apparatus, and should be reported to the laboratory where the apparatus has been prepared so that steps may be taken to rectify any faults in technique. In cases of severe rigor, the transfusion should be stopped and the patient may require an injection of morphine. In less severe cases the reaction ceases if the drip rate is slowed for a while. *Urticarial reactions* complicate about 1 per cent. of transfusions. Their incidence can be kept to a minimum by not accepting as donors those who give a history of frequent urticaria. In some instances the recipient has been subject to urticaria previous to transfusion. When this is the case an antihistamine preparation or ephedrine should be given as a prophylactic. An urticarial reaction occurring during transfusion will usually

subside promptly following an injection of 8 minims (0.5 ml.) of solution of adrenaline hydrochloride B.P.

The severe complications of transfusion include *air embolism* and *circulatory overloading*. Death from air embolism has occurred when positive pressure was applied to a bottle of blood by means of a Higginson's syringe. The presence of fibrin clot converted the blood filter inside the bottle into a cylinder, which permitted an inrush of air through the blood-line although the blood bottle was little more than half empty. This accident can be prevented if positive pressure is never applied after the level of the blood in the bottle has reached the top of the filter. Those who are ignorant of the potential dangers should be forbidden to apply positive pressure. The steps necessary for the prevention of circulatory overloading have been outlined above. Should this complication occur it is best treated by venesection.

Transmission of disease.—Certain diseases may be transmitted by blood transfusion. Donor blood should be Kahn or Wassermann tested on every occasion before transfusion, and any sero-positive blood rejected. Serological tests for *syphilis* will not, however, eliminate all donors who have the disease, the most dangerous being those who are recently infected and whose blood is tested before the reactions become positive. The *Treponoma pallidum* does not survive refrigeration for three days, and in consequence the best preventive against transmission of syphilis is the employment of stored blood. The transmission of *malaria* can be minimized by not accepting as donors those who have experienced clinical symptoms of the disease during the preceding ten years. *Hæmatogenous hepatitis* is referred to in the discussion of plasma transfusion.

Hæmolytic reactions.—A hæmolytic reaction may result from the transfusion of hæmolysed blood, e.g. blood which has been frozen, overheated or grossly infected, or which has been stored too long. This may be termed extravascular hæmolysis and should be entirely preventable. Intravascular hæmolysis occurs when the red cells transfused are incompatible with the recipient's serum or, more rarely, following the transfusion of group O blood to a recipient of group A, B or AB. In this latter instance anti-A or anti-B agglutinins are present in the transfused group O blood in a sufficient concentration to react with and hæmolyse the recipient's corpuscles. A hæmolytic reaction should be suspected if a transfusion is accompanied or followed by any or all of the following: a rigor with pain in the loins, jaundice, hæmoglobinuria, oliguria, absence of increase in hæmoglobin or red cell count.

Intravascular hæmolytic reactions arise mainly because of errors in the grouping and matching of blood, or because of omission of direct matching or grouping owing to undue haste. Sometimes they have arisen through failure to check the bottle label carefully, which would have shown the wrong blood to have been collected from the blood-bank refrigerator.

The grouping and matching of blood should be undertaken by trained and experienced workers only. A clinician who is likely to have to perform these

tests should first undergo instruction. Danger of incompatibility is minimal if the ABO and Rh groups of both donor and recipient are determined by a reliable method and blood homologous in the ABO and Rh systems is transfused. The risk of reaction is greatest in certain patients who might be termed "dangerous recipients". These are patients who have had a reaction to a previous transfusion, and women who have borne stillborn or jaundiced babies. Whenever circumstances permit, blood for dangerous recipients should be selected and matched by a laboratory devoted to this problem, such as a regional transfusion laboratory. In emergency, plasma or saline should be transfused until matched blood can be obtained. Direct matching by a simple slide or saline method will not exclude Rh incompatibility with any certainty. An albumin method must be employed, and blood for the dangerous recipient should be matched by both the albumin and Coombs methods.

The treatment of a hæmolytic reaction should be based on a controlled attempt to hasten the removal of hæmoglobin *via* the kidneys, but should this not prove possible because of renal tubular damage, steps should be taken to provide optimal conditions for regeneration of the damaged tubular epithelium. When the condition is recognized within twelve hours of the transfusion, 100 ml. of 3.8 per cent. trisodium citrate should be injected intravenously to alkalinize the urine, followed by a litre of water by mouth, or one litre of 5 per cent. glucose in water intravenously. If the transfusion is being given to correct oligæmia it should be continued with compatible blood or plasma. Should suppression of urine persist despite these measures, no further attempt must be made to secure a diuresis. Water, salt and protein intake must be carefully controlled and supervised in accordance with the recommendations made by G. Bull *et al.* (1949). In the past many patients with severe hæmolytic reactions have died as the result of the administration of an excessive amount of fluid and alkali during the phase of urinary suppression.

THE RH FACTORS

Besides the A, B and O substances, human red cells contain a combination of antigens known as the Rh factors. Six principal factors have been identified, and are indicated by the letters C, D, E, c, d, and e. Other Rh variants have been designated C^w, D^u, and so on. Fortunately, only one of these factors complicates transfusion therapy with any frequency. This is the D antigen. It was the factor first discovered and described, and is the antigen referred to when a patient is described as "Rh-positive" (i.e. D-positive) or "Rh-negative" (D-negative). The red cells of six of every seven persons contain the D factor and are therefore termed D-positive. The remaining one in seven persons are known as D-negative. These latter may react by forming Rh antibodies, anti-D, should D-positive red cells be injected into their circulation. This is a process of immunization. It may result from a transfusion or intramuscular injection of D-positive blood, or a D-negative

mother may form anti-D should she bear D-positive children.

The D factor may complicate transfusion in two ways. In the one instance, the D-negative patient who has developed anti-D will suffer an incompatible transfusion should he receive a transfusion of D-positive blood. Only D-negative blood will be compatible. In the other, a more subtle process is at work. Most D-negative women do not form anti-D until they have borne several D-positive children. Once these antibodies have formed, however, they pass across the placenta to the fœtus, react with the fœtal red cells and cause hæmolytic disease of the newborn. The transfusion of a single bottle of D-positive blood to a D-negative woman is a more potent stimulus to the formation of anti-D than the bearing of several D-positive children. Thus, the transfusion or intramuscular injection of D-positive blood to a D-negative girl or woman may result in her first baby being affected with hæmolytic disease in its severest form. These facts must be borne in mind by all who practise transfusion, and D-positive blood (i.e. Rh-positive blood) must not be given by transfusion or intramuscular injection to a female patient unless she is known to be D-positive.

The clinical importance of the other Rh factors lies in the fact that in a smaller number of instances (amounting to 1 to 2 per cent. of all cases of Rh immunization) they may stimulate the formation of Rh antibodies of the type anti-C, anti-E, and so on. Fortunately, immunization from these antigens is not sufficiently frequent to necessitate determination of the C or E type of the blood to be transfused when a female is to receive her first transfusion, as is necessary for the D factor. The blood of patients who have had previous transfusions, or women who have borne children may, however, on rare occasions contain anti-C, anti-E, or one of the other Rh antibodies, but incompatibility from this cause may be excluded by matching blood for transfusion by the albumin or Coombs method.

BLOOD SUBSTITUTES

Because of the limitations and difficulties of storage of whole blood, and also because of the complications of grouping and matching, a search has been made for many years for a satisfactory blood substitute. In a case of hæmorrhage, such a substitute is mainly required to restore circulating blood volume until the patient's own plasma protein can enter the circulation. Isotonic salines have proved unsatisfactory because they leave the circulation too rapidly, and they were superseded during the first world war by "gum-saline". The infusion of gum-saline has been criticized, however, on the ground that the gum is stored in the body, particularly in the liver, and that it interferes with liver function. Other colloids investigated, such as pectin, methyl cellulose, polyvinyl alcohol, and polyvinyl pyrrolidone show similar storage phenomena. Human plasma and serum, when stored in the dried form, have proved to be valuable substitutes for whole blood. They do not contain the blood group antigens, and their anti-A and anti-B agglutinins

can be inhibited by suitable pooling during preparation. In consequence, they can be transfused to patients irrespective of blood group.

Human plasma.—Plasma may be prepared from outdated blood, or as a by-product from the preparation of red cell concentrates. It is therefore available in greater quantity than is serum. In the dried state it is stable for at least five years, provided it is stored at a moderate temperature (40° to 70° F.) and not exposed to direct sunlight. It is reconstituted by adding pyrogen-free distilled water. Should reconstitution not be complete within a few minutes, storage has been unsatisfactory and the plasma should not be transfused.

Plasma may be transfused as a blood substitute while blood is being grouped and matched, and is particularly indicated for patients with burns or crush injuries when oligæmia has resulted from plasma loss. Unfortunately, the transfusion of certain batches of plasma is followed by hepatitis in the recipient. This type of hepatitis, known as hæmatogenous hepatitis, has an incubation period of from one to six months and is sometimes fatal. Following the transfusion of "large pool" plasma the incidence of hepatitis has been as high as 10 to 12 per cent. Clinical trials of "small pool" plasma indicate that a reduction in the number of bloods pooled when preparing plasma may reduce the incidence to 1 to 2 per cent. The risk of hepatitis following a transfusion of whole blood or concentrated red cells is about 0.5 per cent. The virus responsible is probably allied to the virus of infective hepatitis, and as a result persons who have had infective hepatitis should not be accepted as blood donors until two years after they have recovered from the attack. Experiment suggests that irradiation by ultra-violet light may sterilize the plasma. Until this can be accomplished, plasma should be transfused only when the danger of withholding the transfusion outweighs the risk of subsequent hepatitis. When a case of hæmatogenous hepatitis is diagnosed, the batch number of the bottle of plasma transfused should be notified to the Regional Transfusion Service so that any remaining plasma of this batch may be withdrawn from store.

Dextran.—Dextran is the latest and most promising plasma substitute. It is a polysaccharide synthesized by bacterial action from sucrose, and was first used as a transfusion fluid in Sweden. A clinical trial recently undertaken in this country (J. Bull *et al.*, 1949) suggests dextran to be as beneficial as plasma in cases of burns, and in the treatment of surgical shock and hæmorrhage. It would appear to be non-toxic and non-antigenic. The ultimate fate of dextran in the body is not yet certain, however, and while this remains in doubt, it is felt that dextran cannot be recommended unreservedly for widespread use.

References

Bessis, M., and Bernard, J. (1947): *Bull. Acad. Méd., Paris*, **131**, 615.
Bull, G. M., Joekes, A. M., Lowe, K. D., and Evans, B. (1949): *Lancet*, **ii**, 229.
Bull, J. P., Rickets, C., *et al.* (1949): *Ibid.*, **i**, 134.

REVISION CORNER

TICS AND THEIR TREATMENT

NERVOUS tics or habit spasms are easily recognizable in their common forms. They occur in both sexes and consist of simple or complex movements, generally purposive in origin, but by constant inapposite repetition rendered useless, stereotyped and almost irresistible to the victim.

VARIETIES OF TICS

The most common simple tic movements are those of the face, neck and shoulders. Blinking, raising the eyebrows, pouting, biting, licking, sniffing, grunting, coughing, nodding, twisting the neck, shrugging a shoulder—all these are familiar enough. Tics of the limbs, chiefly hand movements, may also be seen and often take the form of tapping, rubbing or scratching.

On the borderland of tics are a number of conditions such as the rhythmic movements and fidgetiness of small children, the mannerisms and obsessional acts and utterances of older subjects. The so-called "rhythmias" consist chiefly of head-rolling, head-shaking and head-banging. These and other rhythmic movements, monotonously repeated and apparently both purposeful and pleasurable, may be seen in the first two years of life. In most cases they disappear spontaneously thereafter and require no treatment. They may, however, be prominent and persistent in mental defectives.

Fidgetiness of a diffuse kind is so common in children of pre-school age as to be of little significance. In older children general fidgetiness is almost always an indication of emotional maladjustment and calls for an inquiry into environmental factors. Certain "bad habits", such as thumb-sucking, nail-biting, nose-picking and masturbation, are related to tics. If they occur to excess they may betoken an underlying emotional immaturity or instability.

Vocal tics may be wordless noises or barks, particularly in the condition of generalized convulsive tic (Gilles de la Tourette's disease) or they may take the more obsessional form of compulsive repetition of certain words (echolalia and palilalia) or compulsive utterance of some obscenity (coprolalia). These socially distressing states are rare: fortunately so, since medical treatment is singularly unsuccessful.

Little need be said of mannerisms which are normally to be observed in many people. These may take the form of ritual behaviour, often in private, or of gestures or other tricks of behaviour or speech, particularly in public. So far as these are socially tolerable, they need not be regarded as obsessional states or tics and deserve no further attention.

DIFFERENTIAL DIAGNOSIS

Other types of involuntary movements have to be distinguished from tics. Sydenham's chorea, which seems to be getting much less common, is differentiated by the more continuous, fragmentary and changing character of the movements, by the choreic hand and tongue, the tendency to sighing, and the pronator sign. No original purpose can be discerned in choreic movements and they are never repeated in the same stereotyped way, as are tics. Choreics, like tiqueurs, are commonly of a nervous disposition and occasionally a tic may be derived from a pre-existing choreiform movement.

Huntington's chorea is distinguished by the continuous athetotic character of the movements, as well as by the usual dementia and family history. Hemichorea or hemiballismus, bilateral athetosis, torsion-spasm, progressive hepato-lenticular degeneration (Wilson's disease), and encephalitis lethargica are other uncommon conditions in which involvement of the basal ganglia results in involuntary movements of a distinctive kind. The postencephalitic is particularly liable to develop bizarre involuntary movements superimposed upon an extrapyramidal syndrome; many of these movements have the quality of true tics. The rare paramyoclonus multiplex, the commoner myoclonic jerks which may occur in epileptics between fits, and the occasional involuntary movements, such as fluttering of the eyelids or rubbing of a finger, seen during *petit mal*, need only passing mention. "Tic douloureux" is of course not a tic at all but simply a wincing of the face from the sudden pain of trigeminal neuralgia. Some irritative spasm of the facial muscles may follow an imperfectly resolved facial palsy.

THE NATURE OF TICS

The pathogenesis of true tics is uncertain. Many, particularly in children, may be regarded as a manifestation of transient emotional unrest. Some adults develop a tic based on an occupational movement, when there is pronounced underlying anxiety or weariness. In others the tic is a compulsive feature of an obsessional state. Some movements, such as intractable spasmodic torticollis, are so suggestive of a fragmentary striatal syndrome that an organic basis for them has been suggested, although no morbid histological findings have been recorded. In almost all cases there is evidence of predisposition to neurotic illness and sometimes another member of the family has suffered from a tic. Tics are accentuated by anxiety and are therefore most evident when a patient appears in public or for an interview. As anxiety is allayed the tic diminishes and in sleep it disappears. A sudden emotion or distraction may also temporarily arrest it. It can usually be inhibited for a short time by a strong effort of will, but too violent or prolonged an attempt will aggravate it.

TREATMENT

Treatment must in the first place be directed at improving the psychological adjustment of the tiqueur to his environment. Many tics of childhood are best ignored, but in other instances the attitude of parents or teachers may be at fault; the child may lack the companionship of children of his own age or may have no opportunities for suitable recreation. Fussing or nagging the child must not be permitted. A complete change of environment for a time may be advisable and the provision of a nourishing diet and open-air activities should be encouraged. The great majority of childhood tics respond readily to simple measures on these lines without recourse to sedatives.

The older the patient and the more "fixed" the tic, the more unsatisfactory is the response to treatment. Isolation behind screens in hospital has been used in the past but achieves little. Rest and relaxation are, however, of importance and it is often helpful to begin treatment with sufficient sodium amytal, nembutal or other suitable barbiturate to keep the patient in a drowsy state for the first two or three days. Various "exercises of control" have proved helpful; the patient is taught to relax and then to strengthen his power of inhibition by gradually lengthening lessons. Breathing exercises, accompanied by rhythmic movements of the limbs, and "mirror drill' (which consists in carrying out symmetrical movements of the

two sides of the body) may all assist in re-education of the uncontrolled part. Diversional occupational therapy is also of value in appropriate cases.

Sometimes a tic has its origin in a constantly repeated occupational movement, and this is often the case in somewhat obsessional individuals who have worked for many years at one dull job. So-called "writers' cramp", some forms of torticollis and other movements of the limbs belong to this class. In such cases the patient must be removed permanently from his occupation, for the trouble is almost certain to be perpetuated if he remains at it.

It may be thought that such methods aim only at the removal of what is in effect an hysterical symptom without adequately investigating and treating the underlying cause. The Freudian conception of a tic as a symbolic representation of a repressed impulse demands a psychoanalytical approach. The analysis may be carried out by various techniques and may reveal considerable underlying mental conflict, but the process seems rarely to achieve much success in the removal of the tic. The increased introspection sometimes makes it worse. This is not to say that the psychological setting should be disregarded, since it is often the patient's sense of personal failure or frustration which is the basis of his unrest. Simple discussion, reassurance and suggestion may achieve considerable improvement in his outlook, and this approach to the problem is essential.

Regular drugs have little place in the treatment of tic, but an occasional daily sedative or hypnotic at night may be required.

SURGICAL MEASURES

There are a few special cases in which psychological and general medical measures achieve little or nothing and surgical treatment may be considered. Blepharospasm and blepharoclonus perhaps offer most hope of success to the surgeon. Division of the branch of the facial nerve supplying the orbicularis oculi muscle may stop the tic and yet not prevent the patient from closing his eyes voluntarily. One cannot help wondering how far psychological factors enter into this, particularly as on one occasion I have seen blepharospasm almost completely abolished although histological examination of the material removed showed it to be only connective tissue. In other instances the tic is removed only at the price of a partial facial palsy.

Many surgical procedures have been carried out in an attempt to relieve the tonic and clonic spasm of torticollis. Division of the sternomastoid muscle or the spinal accessory nerve is useless owing to the large number of other muscles which tend to be involved. More complete operations have been performed but, although some enduring successes have been reported, surgical measures should be considered only when other methods have failed, since the results from cutting the nerves and roots are usually disappointing.

For multiple tics with much associated anxiety leucotomy has occasionally been employed and I have seen remarkable improvement in such a case. This operation has, of course, no place in the treatment of the simple forms of tic.

CONCLUSION

Nervous tics are thus a heterogeneous group in which both psychological and neurological factors may be concerned. In many cases, particularly in children, the problem is often a simple psychological one and the prognosis good. In others there may be a profound obsessional basis, much more resistant to treatment.

In others again, it seems possible that, in addition to a defect of personality, there is an organic basis to the involuntary movements, and these are the most difficult to help.

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THE CHOICE OF AN OPIUM DERIVATIVE

THE therapeutically useful constituents of opium and the substances formed from them fall into two groups of alkaloids differing fundamentally in their chemical constitution, their pharmacological actions and their uses in medicine; namely, a group containing morphine and codeine, in which a phenanthrene ring and an isoquinoline ring are intertwined, and a group of benzyl isoquinoline derivatives represented by papaverine. These two groups must be considered separately, the second cursorily, as no member of it is of great importance in medicine.

THE MORPHINE GROUP

Of the group to which morphine belongs, morphine itself occupies such an outstanding place that the other members may best be viewed against a background of its advantages and disadvantages. In medicine, the most valuable properties of the morphine alkaloids are their capacity to relieve pain, anxiety, dyspnœa and cough. All these powers morphine has in full, and it is to find a substance lacking its disadvantages that the search for morphine substitutes has been made. The most serious disadvantage, and the one which interferes most with its use, is its capacity to lead to addiction; and so far a morphine derivative without this capacity and yet capable of replacing morphine has not been found. Other disadvantages are the establishment of tolerance necessitating progressively larger doses, and its effects on the respiratory and vomiting centres and on the alimentary canal.

For an understanding of the action of morphine on the central nervous system it is necessary to realize that it produces a mixture of stimulation and depression. In man the general effect on the higher centres is one of depression leading to quiescence; but in some animals and occasionally in man, excitement may result, possibly explicable by diminished restraint; and for patients with this idiosyncrasy an alternative drug is required. Depression of the respiratory centre, by diminishing the respiratory volume, may lead to inadequate oxygenation; and nausea and vomiting are common and unpleasant side-effects. The changes in the bowel are produced locally and are complex, but principally consist of an increase in muscle tone and a decrease in peristalsis. This leads to a delay in the emptying of the stomach and a slowing in the movement of the contents of the small and large intestine. More fluid is absorbed and the fæces tend to become harder. All medicinal morphine derivatives have this effect, although some, e.g. codeine and dilaudid, to a less extent. Morphine also causes an increase in tone in the plain muscle of the biliary and urinary tracts, leading to a rise in biliary and ureteric pressure. Thus relief from biliary and ureteric colic achieved by the central action of morphine must, to some extent, be offset by this rise in pressure.

Because of the risk of the development of addiction, morphine should be used only in those cases in which (1) no non-habit-forming drug is adequate; (2) the period over which administration will be required is brief; or (3) a fatal outcome

in the near future is inevitable. Opium alkaloids should not be used to promote sleep unless this is disturbed by severe pain. For insomnia the barbiturates are more effective, and when pain is moderate, physeptone or pethidine are preferable, although both can cause addiction.

Many morphine derivatives have been prepared and tested and the properties of a few of the clinically more valuable ones will now be reviewed briefly.

Diamorphine hydrochloride (heroin) has been much used as an alternative to morphine for the relief of pain and cough because it has less effect on the intestinal tract. Addiction develops with it more rapidly than with any other drug and leads to a greater degree of moral degeneration. In 1931 the League of Nations Expert Committee decided that its usefulness did not compensate for its dangers, and since then it has been banned in 26 countries. Experience has shown that it is not indispensable, and there is little doubt that its use in all countries should be discontinued.

Dihydromorphinone hydrochloride (dilaudid) differs from morphine in that it causes less somnolence and less nausea, vomiting and constipation, whilst its analgesic action is roughly ten times greater. The shorter duration of its action necessitates more frequent administration, and this increases the risk of addiction. With analgesic doses, respiratory depression is as marked as with morphine, and it is as effective in the relief of cough. It is a useful substitute for morphine for the relief of pain or cough in those individuals who have an idiosyncrasy to morphine or when it is nauseating. The average analgesic dose by mouth or hypodermically is 2 mg. A prolonged effect can be obtained by the use of rectal suppositories.

Codeine phosphate is weaker than morphine in all its depressant powers, and although addiction occurs this is much less common, as only with large doses parenterally is marked euphoria produced. Codeine is particularly valuable for depressing the cough reflex and may be adequate to relieve moderate pain, although for this purpose the non-opiate analgesics referred to above are usually preferable. Its stimulant action is more marked than that of morphine and doses in excess of 65 mg. tend to cause restlessness.

Ethyl morphine hydrochloride (dionine), chemically closely related to codeine, resembles it in its central actions and has no advantages over it. It has been used as a local application to the conjunctiva to produce hyperæmia and œdema in the treatment of conjunctivitis, corneal ulcers and inflammatory conditions of the uveal tract.

Dihydrocodeinone bitartrate (dicodid) is a useful cough depressant with a prolonged action. It is more potent than codeine but also more addictive, occupying a place between codeine and morphine: dose by mouth, 5 mg.

Methyldihydromorphinone (metopon) and *dihydrodesoxymorphine* (desomorphine) are not yet available in this country. Both have roughly ten times the analgesic power of morphine and correspondingly greater toxicity. They disturb the alimentary canal less than morphine but are equally drugs of addiction.

THE BENZYL ISOQUINOLINE GROUP

Of the benzyl isoquinoline group, *papaverine* is the only member which need be discussed. It is only feebly narcotic and analgesic but, unlike morphine, decreases the tone of plain muscle. As a vasodilator it has been employed in the treatment of coronary thrombosis, angina pectoris and hypertension, and as a spasmolytic in intestinal and biliary colic. It is not habit-forming, and in medicinal doses is

harmless but of very doubtful value. Like quinidine it decreases the conductivity and excitability and prolongs the refractory period of heart muscle, and can be used in the treatment of paroxysmal tachycardia and to diminish the frequency of extrasystoles: dose: 2 to 4 grains (0.13 to 0.25 g.) by mouth; ½ to 1½ grains (0.032 to 0.1 g.) by intravenous injection.

The analgesic action of *opium* corresponds to its morphine content (10 per cent.), but it is slightly more constipating and there is insufficient papaverine in it to modify appreciably the action of the morphine. There is thus no advantage in the use of preparations of opium over those of morphine, except for the action on the bowel. Nor is there convincing evidence that preparations such as Papaveratum B.P.C. (omnopon, pantopon), containing mixed opium alkaloids, are preferable to morphine.

CONCLUSION

In spite of the great volume of work on synthesizing and testing morphine derivatives, morphine and codeine retain their place. In special cases in which side-effects with morphine are marked, dihydromorphinone may be preferable as an analgesic and dihydrocodeinone for the suppression of cough, but the most promising recent development in the relief of pain has been in the production of non-opiate analgesics, such as pethidine and physeptone.

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NOTES AND QUERIES

Vasomotor Rhinitis

QUERY.—I should be grateful for an authoritative opinion on the following points:—

(1) What is the modern opinion regarding the value of skin tests in a case of vasomotor rhinitis, to determine the sensitizing agent or agents?

(2) What is the hope of obtaining relief for this rather distressing complaint by desensitization? I am under the impression that these subjects may react positively to so many agents as to render attempts at desensitization valueless.

(3) Is cauterization of the nose of any value in treatment?

The patient in question has an allergic family history and has other manifestations of allergy, e.g. suspender rash and a localized dermatitis on the wrists caused by wearing a wristwatch. X-ray of the sinuses reveals a mucous polypus on the floor of the right antrum about the size of a cherry; this has been present, to my knowledge, for at least three years and does not vary in size, and there are no symptoms suggestive of antral infection. Could this polypus have anything to do with the causation of the symptoms? The patient is unfortunately unable to take any of the antihistamine drugs owing to the severity of side-effects, e.g., excessive drowsiness and lack of appetite, which symptoms are present in a marked degree when taking only one tablet a day.

REPLY (1).—(1) Experience often shows that in cases of vasomotor rhinitis skin tests point to a large number of agents being responsible.

(2) On the whole, except in very occasional cases, treatment by desensitization is disappointing.

(3) Cauterization of the nose quite often gives relief in these cases, at any rate for a time.

(4) It is doubtful whether the mucous polyp in the floor of the antrum plays any part in producing the symptoms. Such polypi are not uncommon in cases of allergic rhinitis.

W. A. MILL, M.S., F.R.C.S.

REPLY (2).—Skin testing is an essential part of the investigation of a case of vasomotor rhinitis. Provided the tests are carried out with reliable reagents, and the results interpreted by an experienced worker, the reactions are of great assistance in arriving at the specific diagnosis. Apart from pollen allergy, multiple sensitization is more common than single sensitization. As with all clinical pathology, such tests are only *aids* to diagnosis, and it is the *correlation* of skin reactions with clinical sensitivity which is the basis of accurate specific diagnosis and successful treatment. Not all cases of vasomotor rhinitis are due to allergy to extrinsic allergens:

any cases are due to sensitization to a low-grade infection in the upper respiratory tract, and some to reflex irritation from nasal abnormalities, such as a deflected septum. In selected cases, specific avoidance of the causal allergen(s), or specific desensitization, gives excellent clinical results. Cauterization and other surgical operations on the allergic nose have a place in treatment, but are rarely justified as the first step in treatment owing to the risk of asthma developing, and they should usually follow a course of desensitization therapy.

In the case cited, the antral polypus is unlikely to be of causal significance in the present complaint, although it is itself probably the result of the allergic process active in the patient; there seems to be no indication for its immediate removal. With the range of antihistaminic drugs now available, it is unusual to find a patient who cannot tolerate at least one preparation in minimal dosage, although it should not be difficult to neutralize undesirable side-effects by using complementary doses of caffeine, ephedrine or amphetamine.

The adequate investigation of a case of vasomotor rhinitis should include coordinated skin testing, ear, nose and throat examination, and a bacteriological overhaul of the upper respiratory tract, before the specific diagnosis can be established with any reasonable degree of certainty, and a rational scheme of treatment evolved.

DAVID HARLEY, M.D., F.R.I.C.

DDT and Ant Control

QUERY (from a subscriber in Trinidad).—The destruction of ants is an important problem out here, and I should be grateful if you could let me know whether either DDT powder or "gammexane" is lethal to ants? What is the best way of applying these preparations for this purpose?

REPLY.—DDT and *gamma* BHC ("gammexane") are toxic to various kinds of ants as they are, in different degrees, to all insects against which they have been tried. Their practical effectiveness and the best method of using them depend upon the particular nature of the infestation. The question does not state what kind of ant is causing trouble nor whether the nuisance is in the house or the garden; it is presumed that "white" ants (termites) are not involved.

Against ants in the house, spraying to leave residual deposits of DDT is often effective. Considerable numbers of workers are killed, but the colony is not destroyed and eventually revives. Repeated poison baiting, e.g., with 0.5 per cent. sodium fluoride in syrup, is more effective in the long run, although it may need to be continued for as long as two months. As regards garden pests, there is a report on the successful use of DDT against ants damaging a lawn. DDT dust, 10 per cent., was scattered at the rate of 1 to 8 g. of DDT per square yard and achieved good control in about five weeks with the lowest dosage. The heavier dosage was more rapidly effective. On all questions of ant control it must be remembered that by far the best method is to trace the nests, dig them up and destroy the brood (boiling water, paraffin or carbon tetrachloride). Killing large numbers of workers alone may not exterminate the colony. One Pharoah's ant infestation in a hospital in England was attacked for two years by trapping the wandering ants. During this time some 5½ million workers and 6000 queens were killed without eliminating the infestation.

J. R. BUSVINE, D.SC.

Loss of Hair after Childbirth

QUERY.—What is the best treatment for generalized falling of the hair in a woman aged thirty following a recent pregnancy? I understand that Sabouraud described this condition and stated that lactation could delay the fall until after weaning. The patient's general condition is excellent; there is no evidence of nervous instability. On examination the hair is dry and the ends are split. The patient is afraid to brush the hair too strenuously because it is falling so rapidly. Her hairdresser recommended a course of treatment which involved applying a special cream to the scalp and providing the necessary temperature by using a thermostatically controlled cap. Has this treatment any value?

REPLY.—Diffuse hair-fall, when it occurs as a sequel to childbirth, usually takes place during the ninth week after parturition. The reason for this fairly constant latent period is obscure but it is unlikely to be related to lactation, for a similar delay occurs in symptomatic alopecias following a pyrexial illness or severe constitutional disturbance, which mostly do not become manifest until well into convalescence. The hair throughout the scalp may then loosen and come out with alarming rapidity, as is evidently happening in the present case. The prognosis in symptomatic alopecias, however, is almost invariably good and the patient can be reassured that spontaneous and complete regrowth may be expected. Thus active treatment to the scalp is unnecessary; indeed, it may be unwise, for overstimulation while the hairs are still loose may cause acceleration or extension of the alopecia.

I have no knowledge of the particular treatment mentioned in the question but, in common with other local remedies for alopecias, its object presumably is indirectly to influence the hair

papillæ by increasing the circulation in the scalp. The ineffectiveness of such methods has been made only too evident of late by the many bald and partially bald persons appearing at skin clinics in quest of wigs.

E. W. PROSSER THOMAS, M.D.

Keloid after Vaccination

QUERY.—I vaccinated a young woman aged twenty about ten months ago during a smallpox scare. She had never been vaccinated before and the method used was the multiple pressure technique over the deltoid insertion. She "took" satisfactorily; it scabbed well and caused little or no trouble until about six months ago, when the resulting scar became intensely irritating. On examination the scar was smooth, red and shiny, raised, and with fine capillary markings; size about that of a small pea. I told her not to worry about it as it would go away, but unfortunately if anything it is increasing in size and irritability. Local applications do not help. It looks most ungainly with short-sleeved frocks and she is very concerned. From the same batch of lymph I vaccinated five other patients in the same household and their scars have settled down completely. What might this be? Could it be a keloid? Might it be due to secondary infection? i.e. pus beneath. Can I incise through the scar?

REPLY.—From the description given this appears to be a keloid, which is an uncommon complication of vaccination and is not caused by any peculiarity of the lymph or defect in the technique of insertion, but is associated with the tendency of certain individuals towards overgrowth of scar tissue after any trauma to the skin. Incision or other surgical treatment of a keloid would probably be unwise, but this disfiguring condition might be much improved by an application of X-rays. For this purpose the patient should be referred to a specialist in radiotherapy.

E. T. CONYBEARE, M.D., F.R.C.P.

Post-Abortal Infection

QUERY.—Two weeks ago my wife had an abortion which became septic from retained placental fragments. The illness was quickly controlled with penicillin and the sulphonamides. Since then, however, she has been conscious of distension and discomfort with pain on pressure over both Fallopian tubes, and on three occasions a watery (?) pus has escaped per vaginam. I take it that she has intermittent hydrosalpinx, although the gynæcologist who saw her, and examined her most carefully, assures us that there is nothing to be felt. The patient is very well and her local medical adviser allows her up for several hours every day, although this d comfort still persists and she is only comfortal lying on her back in bed. What further tre ment would you advise? Would one be justifi in trying streptomycin?

REPLY.—The symptoms described suggest continuing mild infection in the pelvis. As gynæcologist has recently examined the pati one presumes that any marked salpingitis h been excluded, and as there has been a g response to penicillin it would not se necessary to try streptomycin. At this stage patient could probably derive most benefit fr heat applied locally to the lower abdomen by electric pad. Another course of penicillin co be given. It is not stated whether the aborti was complete; there may be discharge from t uterus if it has not been complete.

KENNETH BOWES, M.D., M.S., F.R.C

Hypertrichosis in a Child

QUERY.—A child patient of mine, aged th years, has a large amount of hair on her ba arms and legs. Is it advisable to do anything the way of treatment? Would some glandul therapy be likely to effect a cure?

REPLY.—The causes of excessive hairin (hypertrichosis) are various and mostly u known. Classifications of the varieties of t condition have been attempted, not usually an etiological basis, but on the distribution a character of the excessive hair and the age a sex of the subject. If the subject of this questi a child of three years, is in all other respe normal, the condition is almost certainly not d to any *known and treatable* endocrine d turbance. I would advise no action and wou give a guarded prognosis. For further deta see Danforth, C. H. (1925): *Arch. Derm Syph., Chicago.*, **12**, 380.

A. DOYNE BELL, D.M., F.R.C.

Voluntary Patients and Certificatio

QUERY.—A patient of mine is a voluntary i mate in a private mental home. If a Receiver appointed, will this patient, as a consequence appointing a Receiver, have to be certified insane?

REPLY.—A voluntary patient does not require be certified if a Receiver is appointed. A patie may still wish to be resident in a mental hospit and at the same time realize that he is not ab to look after his affairs, and the Courts are qui willing to cope with such an application, on the necessary affidavits are completed.

HENRY WILSON, M.D., F.R.C.

PRACTICAL NOTES

Aureomycin in the Treatment of Herpes Zoster

A REPORT of the use of aureomycin in the treatment of herpes zoster is given by M. L. Snyder and L. E. Stubbs (*Journal of the American Medical Association*, December 10, 1949, **141**, 1050). 500 mg. of aureomycin was given six-hourly for two days to four patients with herpes zoster. In three cases the results were dramatic: there was relief from pain within twenty-four hours; in two cases the rash dried and disappeared within five days; in one case, in which pain persisted for three to four days, the rash disappeared in seven days. In the fourth case, that of an eleven-year-old girl, with temperature of 102° F., 250 mg. of aureomycin were given six-hourly; there was dramatic relief of pain within twenty-four hours and no further elevation of temperature; the rash subsided within four days. Unfortunately in this case acute poliomyelitis developed five days later. The authors state that it was by accident that the possible beneficial effects of aureomycin in herpes zoster were made known to them: a patient receiving X-ray therapy for herpes zoster was given aureomycin for another condition, and within twenty-four hours there was dramatic relief of the herpes; it was not known whether this was due to the X-ray therapy or to the aureomycin. In conclusion it is stated that the report is submitted in the hope that further investigation will produce equally good results in the treatment of a disorder which, in the past, has been so refractory in resisting all forms of therapy".

Trichloracetic Acid Treatment of Bartholinitis

MÉCHIN (*Presse Médicale*, December 17, 1949, **57**, 1169) has treated seven cases of chronic bartholinitis with purulent discharge, in most cases gonococcal, with trichloracetic acid. In two cases the discharge was from the neck of the gland, a form particularly resistant to treatment. Two methods of application were adopted:—(1) Catheterization of the excretory canal, using a needle with filed end, and then injection by means of the same needle of a few drops of saturated solution of trichloracetic acid. (2) A small piece of cotton-wool was fixed to a fine mandrel (for example, the mandrel of an intramuscular needle), soaked in trichloracetic acid, wrung out, and then used to swab the canal of the gland. Either one or other of these methods was employed, or the two methods were combined, the treatment being begun with the first method and finished with the second. A necessary precaution is to protect well the surroundings of the gland orifice in order to avoid burning; this occurs at times in spite of precautions, and particularly with the first method, owing to backward flow of the acid between the needle and the canal walls. Cure was obtained in eight to fifteen days: first the gonococci disappeared, and then the lesions dried up, leaving only some scars in the depth of the canal which were felt on palpation. In one case a cyst was present at the mouth of the canal, the size of a large apricot stone; this was cured in three days by puncture followed by injection of 0.5 ml. of acid. In conclusion the author says: "Trichloracetic acid appears to give results superior to many products employed so far".

Male Subfertility

THE following are the minimum "normal" figures used by the laboratory of the Family Planning Association in assessing the quality of specimens of semen:—

Volume: 1.5 ml.
Density: 40 millions per ml.
Basic motility: 40 to 50 per cent.
Morphology: Total abnormalities not to exceed 40 per cent.; head abnormalities not to exceed 25 per cent
Viability: The motility of the five-hour count should not be less than half the basic motility.
Leucocytes and other cells: Not more than 2 millions per ml.

In discussing the application of these figures in a series of 5,400 semen analyses in 3,182 men, H. A. Davidson (*British Medical Journal*, December 10, 1949, **ii**, 1328) draws attention to certain common fallacies in seminal analysis. For instance, with regard to density it is reported that in a series of 125 pregnancies the minimum densities were three-quarters of a million before, and 1½ millions after, conception. "It would seem unwise to tell a man suffering from oligozoospermia that he is sterile or that he needs no help". The author considers that it is unwise to attempt treatment in cases of total azoospermia and oligozoospermia without first performing testicular biopsy, "a minor operation which can be performed in a few minutes in a consulting room, clinic, or outpatient department". This allows of a decision as to whether azoospermia is due to blockage of the epididymides or vasa (which may respond to surgical treatment) or to failure of spermatogenesis (for which there is no treatment). So far as treatment is concerned consideration is given to two forms of therapy: vitamin E and testosterone. The former was used in 42 unselected subfertile men with no appreciable effect, whilst methyl testosterone (doses of 5 mg. on alternate days to 10 mg. daily for four to eight weeks) was given to 53 unselected subfertile men, again

with no appreciable effect. The comment is added that "treatment with the gonadotrophins would still seem to hold out some hope, but reliable figures are not yet available".

Intravenous Histamine in Nervous Diseases

A SERIES of patients with muscular contractions, including disseminated sclerosis, Batten-Marie's hereditary familial ataxia, congenital myotonia, encephalitis with spastic hemiparesis, muscular hypertrophy, and other nervous conditions, have been treated at the Neurological Clinic, Palacky University, Czechoslovakia, by injection of histamine combined with vitamins B_1 and C (M. Serel: *Schweizerische Medizinische Wochenschrift*, December 24, 1949, **79**, 1247). Histamine (Roche) 1 mg., benerva forte 300 mg., and 1 ampoule of vitamin C (10 ml. = 1 g.) were given in 500 ml. of physiological solution, every second or third day according to the tolerance of the patient, the blood pressure, pulse and respiration. The duration of the intravenous infusion was from one-and-three-quarters to two-and-a-half hours. If the rate of infusion was greater than this it was noticed that the arterial pressure and respiration increased rapidly and the pulse rate decreased. The best results were obtained in cases of disseminated sclerosis with pyramidal muscular contractures, improvement being noted sometimes after the first infusion, but most often after the third or fourth. Improvement was also obtained in some cases of hypermetria, tremor, adiadokokinesis and asynergia which had failed to respond to other forms of therapy. The treatment is contraindicated in affections of the heart, disease of the kidneys and liver, and all forms of malignant disease.

Sterilization of Plaster of Paris Bandages

A SUCCESSFUL method of sterilizing plaster of Paris bandages without in any way affecting their serviceability is recorded by R. J. Gibbons and J. Burke Ewing (*Canadian Medical Association Journal*, December 1949, **61**, 618). The method adopted was treatment of the bandages with formalin vapour *in vacuo*; it was carried out as follows:—

Stock plaster of Paris bandages containing natural contaminants and also heavily seeded with *Cl. sporogenes* and *B. subtilis* were treated with formalin vapour *in vacuo* and then transferred aseptically to a sterile fruit sealer containing approximately 300 ml. of Bacot fluid thioglycollate medium and incubated for one week at 36° C. In eight separate experiments none of the bandages so treated showed any growth, whereas unheated bandages showed growth of *Cl. sporogenes* and *B. subtilis* in twenty-four to forty-eight hours. As a further check 24 of the bottles which were sterile after the seven-days' sterility test were inoculated with spores of sporogenes and subtilis: only two showed any growth. It was found that residual formalin from the bandages had diffused into the medium and that a gradual fall in pH of the medium occurs during the seven-day period; this could be circumvented by increasing the volume of the medium to not less than 750 ml., or by using the smaller volume and, after formalin treatment, treating the bandages *in vacuo* with ammonia vapour to inactivate the formalin, and buffering the medium with marble chips. Further tests using the larger volume of medium and artificially contaminated bandages showed the bandages to be sterile, and the media seeded at the end of the tests grew *B. subtilis* and *sporogenes*.

The sterilized bandages were then submitted to clinical trial: used in fifty cases of fracture they proved uniformly satisfactory: they fitted and looked like normal bandages; there was no difficulty in applying them; they set normally and stood up to usual wear and tear; there was no odour of formalin, and no incidence of irritation of the skin. "Bandages treated in the original metal container which, following sterilization, is immediately sealed with waterproof adhesive or Scotch tape and stored in a dry place should remain sterile almost indefinitely".

Oral Manifestations of Acute Leukæmia

IN reporting four cases W. S. Matheson of the Dental Department of Manchester Royal Infirmary (*British Dental Journal*, November 1, 1949, **87**, 265) draws attention to the fact that "oral manifestations in cases of acute leukæmia are of frequent occurrence and their appearance in the early stages of the disease often leads the patients consulting a dental surgeon before the onset of the general malaise". The relevant details of the four cases are as follows: (1) A male, aged twenty-nine, originally consulted his dentist because his dentures were "making his mouth sore". When seen in hospital twelve weeks later there was considerable hypertrophy of the gums with necrotic areas and constant oozing of blood. A blood count revealed the presence of acute monocytic leukæmia. The patient died a month later. (2) A female, aged twenty-three, was referred to hospital by her doctor with the following letter: "She has had a very septic mouth and gums for the past two days, with a temperature around 102° F. The condition has not responded to penicillin lozenges". Examination revealed marked hypertrophy of the gums with extensive and deep ulceration around the teeth. It was not possible to determine whether the diagnosis was acute myeloblastic or acute monocytic leukæmia. The patient died three weeks later. (3) A male, aged thirty, in whom a diagnosis of acute monocytic leukæmia was made, had previously had dental treatment for swelling and bleeding of the gums. He died ten days after admission to hospital. (4) A female, aged fifty-eight, another case of acute monocytic leukæmia, was admitted to hospital because of breathlessness and swelling of the

s and bleeding around the teeth. There was a history of vaginal bleeding. She died two nths later. Attention is drawn to the fact "the view is held by some workers that ertrophy and ulceration of the gingivæ is racteristic of monocytic leukæmia and that diagnosis should be suspected on clinical nds in such cases". It is recommended that lood examination should be made "at an early e in any case of gingival hypertrophy with morrhage of sudden onset which does not pond to local treatment. Surgery should be ided in these cases as it is likely to be fol- ed by intractable hæmorrhage and a rapidly aling infection".

eatment of Urinary Infections in ildren

CORDING to G. B. Logan (*Proceedings of the ff Meetings of the Mayo Clinic*, October 26, 0, 24, 562), sulphathiazole is the best drug the treatment of a child with an infection the urinary tract caused by a gram-negative illus. The dosage is 0.07 g. per kg. body ght every twenty-four hours, given in four to equal doses. The aim of such treatment is maintain an adequate amount of the drug in urine. When the infecting organism is *E. li* it is not necessary to test the pH of the ne during treatment with sulphathiazole. eatment is continued until the urine has been rile for a week. When the infection is due to *reptococcus fæcalis* the drug of choice is ndelic acid, which is also effective against ny strains of *E. coli*. The dose is that amount cessary to maintain a concentration of the ug of 0.5 to 1 per cent. in the urine: the mer is sufficient if the pH of the urine is 5 less; the latter is necessary if the pH is 5.5. uid intake should be restricted to 1000 to 00 ml. daily. A child is more likely to excrete acid urine if milk and fruit juices are omitted m the diet. The dose for a child whose fluid ake is 1,200 ml. and whose urinary pH is 5, 6 g. daily, divided into four doses given six- urly. The article was written before aureo- cin became available, but it is stated that e seldom find it necessary to employ penicillin streptomycin".

enicillin in the Treatment of Burns

THE early administration of penicillin systemic- ly is the most valuable protection available. In ddition to limiting infection, it would appear encourage the early separation of sloughs . . . enicillin should be given intramuscularly in all ep burns, in all burns of the face and hands d in burns of the air passages, either by a con- uous drip method or intermittently every ree hours "(A. B. Wallace: *Annals of the Royal College of Surgeons of England*, November 1949, **5**, 283). In addition to its systemic administration, penicillin is the basis of the treatment of burns by the exposure method, the principles of which are:—(1) "To keep the raw area dry and so prevent the multiplication of surface-containing organisms; (2) to immobilize the part to prevent invasion of the tissues by infecting micro-organisms; (3) to administer penicillin systemically to counter any tendency to general and local infection; (4) to render nursing care as simple as possible". After cleansing the burn, penicillin powder is dusted over it, the dusting being repeated every four hours for the first twenty-four hours, and then when necessary. The patient is nursed in a general surgical ward with a regulated temperature, adequate ventilation, but no draughts. No sulphonamide drug should be mixed with the penicillin powder, owing to the risk of absorption. Penicillin is administered systemically, four-hourly, in dosage of 500,000 units daily, and satisfactory immobilization of the injured part must be ensured. The ward is swept four times in the twenty-four hours and the nurses and surgical staff only wear masks when carrying out the dressings; thus, it is stated, "all manner of organisms must fall on the surface of the burn, yet infection does not supervene". If this method is attempted, however, nursing care must be rigorous, particularly during the first forty-eight hours.

Vitamin E in Intermittent Claudication

A GROUP of 41 patients with obliterative vascular disease leading to intermittent claudication, in whom as criteria for inclusion in the treated series it had been determined that (1) sympathectomy was contraindicated, (2) no other treatment had been administered, and (3) the halting distance did not exceed 500 yards, have been treated with vitamin E (*a*-tocopherol: "ephynal", Roche), and the results are recorded by A. Hall Ratcliffe (*Lancet*, December 17, 1949, **ii**, 1128). A group of 25 patients on placebo treatment was used as control. Large doses of *a*-tocopherol were necessary, the optimum dosage being 400 mg. daily, and this must be continued for some time, as there is some delay before signs of improvement are apparent; in the treated series this was from four to eight weeks, average six weeks. Of the 41 cases treated 34 were improved; this improvement was assessed by the patient's ability to walk more than 880 yards, whereas before treatment they had been obliged to halt at less than 500 yards. Of the 25 patients in the control group, 5 were improved. These results were recorded after a period of three months' treatment.

REVIEWS OF BOOKS

A Textbook of Neuropathology. By Ben W. Lichtenstein, M.D., M.S. Philadelphia and London: W. B. Saunders Company, 1949. Pp. xviii and 474. Figures 282. Price 47*s.* 6*d.*

It is perhaps unfortunate that the term "neuropathology" was ever coined, for it popularly connotes a variety of pathology which is essentially different from general pathology; yet this is not so, for neuropathology is general pathology applicable to one system only and for that reason he or she who would aspire to be a neuropathologist must be primarily a pathologist. It is true that neuropathology demands a greater basic knowledge of the clinical specialty than does the study of special pathology applicable to some other system, bones and joints for instance, or hearts, but the tendency in all branches of pathology is to bring the pathologist into closer clinical contact with his subject, and in neuropathology this means something more than a nominal six months spent in the wards. Dr. Lichtenstein has designed his book for the medical student and for those training in neurology, psychiatry, pathology and neurosurgery; consequently, the orientation of his study is fundamentally anatomical. The introductory chapters are on nomenclature, methodology and pathogenesis, whilst at the end of the book are clinical, neuro-anatomical and technical supplements; the first of these one would have thought unnecessary, although a list of eponyms is always helpful. The book in general is lucid and well written, and at the end of each chapter there is a short, well-chosen list of references. A valuable asset is the collection of illustrations, no less than 282 being included; most of them are of a high quality. There are redundancies in the text which in a subsequent edition might be adjusted with the aid of a cross reference. There are also certain omissions which might be rectified: there is no account of the pathology of streptomycin-treated cases of tuberculous meningitis; kernicterus is referred to, but although its association with icterus gravis neonatorum is mentioned the interesting sequence of pathological events is somewhat perfunctorily dismissed as "the nerve cells initially damaged by ischæmia, anoxia, intoxication, bile salts, etc., become pigmented secondarily". Not only is this confusing to the student but it misses the fact that the underlying disease is one of hæmolysis consequent upon the development by the mother of antibodies against the Rh factor. This is an instance, in fact, of the danger of regarding neuropathology too much as a specialty; the emphasis should be placed on the underlying hæmolytic process. The chapters inflammations, neoplasms, malformations deformities are good, the last of these includ a practical section on herniations, but in chapter on neoplasms some account of the re tive frequency of the various forms of tum would be helpful to the student. The book well produced and pleasing. It will undoubte find a place alongside other textbooks of neu pathology in the laboratory library. Dr. Licht stein is to be congratulated on his work.

The Common Infectious Diseases. By Stanley Banks, M.D., F.R.C.P., D.P London: Edward Arnold & Co., 19 Pp. vii and 354. Figures 90. Price 21*s.*

Initial reaction to an addition to our crowd bookshelves on the common infectious disea will be that this subject is well covered existing publications. After reading this bo however, one can only come to the conclus that Dr. Stanley Banks has assembled material in such an orderly and concise patte as to assure a good reception both from t student and postgraduate. To the busy pra titioner it will afford a reliable and authen reference in case of doubt, with symptomatolo and treatment so clearly expressed. Small poi of comment arise in connexion with the tre ment of the relatively rare condition known acute laryngo-tracheobronchitis of presum viral origin discussed on page 27. No mention made of chloromycetin as a therapeutic measu whereas many clinicians are finding this e tremely useful. Chloromycetin also deser reference in the treatment of whooping-coug The index refers to streptomycin on page 21 whereas no mention of the drug occurs on th page. Author and publishers are to be co gratulated on an excellent contribution.

Practical Lessons in Psychiatry. By Josep L. Fetterman, M.D. Springfield, Illinoi Charles C Thomas; Oxford: Blackwe Scientific Publications, 1949. Pp. ix an 342. Price 30*s.*

There was a time when books on psychiatr were vague and theoretical, and one was le with the impression that case-taking itself w the chief form of therapy. This book, howeve belongs to the American 'get-well-quick-wit physical-aids' school. Unlike some others, it not a mere bibliography of recent literatur but the writer has had extensive experience o the methods he describes. Neurotic patients ar treated with persuasion, suggestion, narco

lysis and group psychotherapy, whilst he also scribes the modern treatment of cyclothymia, izophrenia, psychopathy and the organic choses. Some subjects are less fully treated, h as alcoholism, sexual deviations and in- ations for cerebral surgery. A useful book, icularly for specialists.

xual Development. Vol I. By J. H. PRINCE, F.R.M.S., F.Z.S., F.B.O.A., F.S.M.C. Edinburgh: E. & S. Livingstone Ltd., 1949. Pp. xii and 418. Figures 190. Price 50*s*.

st core of Prince's book deals with the olution of the eye and of the function of ion; but it covers the whole field of com- ative ophthalmology, and comprises also ful chapters on the senses and the meaning of ception, the influence of education, memory, vironment and occupation, and the photo- emistry of vision. Dark adaptation and its re- ion to night blindness are also considered, and re is a practical section on the clinical and roscopical examination of the eyes of mals, and on laboratory methods. While rsuing the story of ocular and visual de- lopment, we are constantly reminded that ry step in such development is related to comitant stages in the evolution of the hole organism, and to changes in habits and in bitat. Perhaps the most fascinating part of the dy is that concerning the evolution of colour ion, and of colouring of the body as a pro- ective mechanism, and the part it plays in sex splay. Colour perception and discrimination the lower animals has been the cause of much ntroversy, but the writer agrees with those ho allow a notable capacity for discrimination f colour in a number of our dumb friends. he author's field is a wide one, but his material well assembled, his style is lucid, and the lustrations are more than adequate.

urther Rare Diseases and Debatable Sub- jects. Edited by F. Parkes Weber, M.D., F.R.C.P., London: Staples Press Ltd., 1949. Pp. viii and 236. Illustrated. Price 25*s*. net.

his supplementary volume to *Rare Diseases nd Some Debatable Subjects* (2nd ed., 1947) ill be read with profit, astonishment, and envy y Dr. Parkes Weber's many friends and ad- irers, who will be grateful to him for as- embling such a wealth of widely scattered terature within the compass of a small volume nd for his erudite and illuminating comments. f the 41 articles, notes, and letters covering the eriod 1921 to 1949, the longest is 27 pages and he shortest half a page. Some are from the editor's pen, some are written in col'aboration, and a few are contributed by other authors. The text does not always make for easy reading, being broken up by references and parentheses, but there are useful summaries and bibliographies. The chapter-headings, although elaborate, are descriptive, and the numerous illustrations are clear and helpful. Apart from an occasional misprint and transposed line, this valuable work of reference is marred by an inadequate index and an Olympian disregard of accepted bibliographic conventions.

Lord Lister. His Life and Doctrine. By Douglas Guthrie. Edinburgh: E. & S. Livingstone Ltd., 1949. Pp. viii and 128. Plates 20. Price 15*s*.

It was inevitable that Edinburgh's own distinguished medical historian should sooner or later write a life of one of his native University's most famous adopted sons. That the task has been well done goes almost without saying. Perhaps his style has been somewhat cramped by the limitations he has imposed upon himself. All Listerian biographers seem to be unable to rid themselves of the respect almost approaching veneration, which they show for Godlee's comprehensive if scarcely inspiring biography. Wisely in the circumstances Dr. Guthrie has devoted himself mainly to Lister's doctrines, merely sketching in his life as a background. The background, however, is most effective and serves to bring out that striking personality which made such an impression on all Lister's contemporaries. There can be few survivors who remember him at all well, but the reviewer's father-in-law, still hale and hearty, who was elected a Fellow of the Royal Society while Lord Lister was President, still retains a vivid memory of Lister as "a kind old gentleman with a benevolent expression". This is certainly the dominating picture one obtains of him from his many biographers, except possibly in his later years when solitude and physical deterioration weighed so heavily upon him. One can well believe that the portrait in the Royal College of Surgeons, beautifully reproduced in colour in this volume, is a brilliant likeness. It is in the same homely benign style that Dr. Guthrie has couched his biography, which will appeal to both laymen and doctors.

Autobiography of Dr. Robert Meyer (1864-1947): *A short abstract of a long life.* With a Memoir of Dr. Meyer. By Emil Novak, M.D. New York: Henry Schuman, 1949. Pp. xvii and 126. Price $2.50.

This is a brief but fascinating account of the long life of a great man. Readers will feel a debt

of gratitude to Dr. Emil Novak by whose persuasive powers Dr. Meyer was induced to write this record of his life and work. When a man in exile can write "I have had an exceedingly beautiful life which would be worth living once more", he is a great man. Robert Meyer wrote these words after being compelled to flee from the land of his birth and the clinics from which he had achieved international distinction by his contribution to scientific knowledge. A man of many parts, Robert Meyer viewed life philosophically with the keen interest and appreciation of a humorist. After an early training in general medicine he directed his energies to gynæcology and gynæcological pathology, and it was to this latter subject that he made his most valuable contributions. He lived in Germany at a time when German medicine was justly renowned and attracted postgraduates from all over the world. His contemporaries and teachers included such famous men as Virchow, Hegar, Veit, Carl Ruge, von Recklinghausen, Hertwig and Bumm, to name only seven, but medicine was not his only interest. He loved good music and was himself an accomplished musician. Literature, the arts and the beauties of nature were all fields in which he revelled, and health and happiness contributed greatly to his appreciation of life and the art of living. This little book of just over 100 pages is as stimulating as it is fascinating.

Blakiston's New Gould Dictionary. EDITED BY HAROLD WELLINGTON JONES, M.D., NORMAND L. HOERR, M.D., and ARTHUR OSOL, PH.D. Philadelphia: The Blakiston Company; London: H. K. Lewis & Co. Ltd., 1949. Pp. xxviii and 1294. Illustrated. Price 45s.

THIS is "a completely new reference work" based upon Gould's Medical Dictionary, which has been a standard work of reference since its inception in 1890. Points of interest are: the use of boldface type for each item with subentries indented in columnar form which facilitates rapid and easy reference; tables of the veins, arteries, muscles, ligaments, bones and joints, with their origin, distribution, and function; the inclusion of many proprietary preparations which have become standardized, and, of course, the incorporation of advances and the names of those from whom such advances have originated, thus adding several illustrious names to medical history. The authors have adopted the principle of indicating pronunciation by syllable division and accent instead of by the use of phonetics. As the work is of American origin so also is the spelling, and the diphthong no longer occupies the place of honour. This is a good dictionary, and well illustrated by a series of plates, some in colour.

NEW EDITIONS

DEVELOPMENTS in the use and production of penicillin during the four years that have elapsed since the appearance of *Penicillin: Its Practical Application*, edited by Sir Alexander Fleming, F.R.C.P., F.R.C.S., F.R.S. have necessitated a number of changes in its second edition (Butterworth & Co. [Publishers] Ltd., 30s.). crystalline penicillin, procaine penicillin, oil and wax mixtures, and new methods of administration. Chapters on toxic manifestations and the use of penicillin in acute infectious diseases and on streptomycin, have been added, and in appendix B a section is devoted to aureomycin. This is a most useful book for the practitioner.

Handbook of Digestive Diseases, by John L. Kantor, M.D., F.A.C.P., and Anthony M. Kasich, M.D., F.A.C.P. is Kantor's "Synopsis of Digestive Diseases" in a new guise for its second edition (Henry Kimpton, 75s.). Not only has the book been entirely rewritten but it is set in a new format, runs to 658 pages, and contains 149 illustrations; it is, in fact, "essentially a new work", in which the many advances in gastroenterology that have taken place since the publication of the original work in 1937 have been incorporated.

IN the third edition of *The Conduct of Life Assurance Examinations*, by E. M. Brockbank, M.B.E., M.D., F.R.C.P. (H. K. Lewis & Co., Ltd., 12s. 6d.) a number of additions to the sections on the forms of insurance and pension schemes have been included. That a new edition has been called for within a year of the appearance of the former one testifies to the practical usefulness of this book.

The Eye and Its Diseases, by 92 International Authorities, edited by Conrad Berens, M.D., F.A.C.S., in its second edition (W. B. Saunders Company, 80s.) appears thirteen years after the first publication, and many advances have taken place during that time. The revolution in the treatment of some diseases of the eye, particularly those due to gonococcal infection, since the discovery and use of penicillin; advances in orthoptics; the surgical treatment of detached retina; gonioscopy; new theories and practices concerning illumination—these are but a few of the additions to a work on diseases of the eye, many of the contributors to which are of world-wide reputation. The new edition contains 436 illustrations, some in colour.

The contents of the March issue, which will contain a symposium on "Diseases of the Skin", will be found on page lxxiv.

Notes and Preparations, see page lxi.
Fifty Years Ago see page lxvii.